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=> file biosis medline caplus wpds uspatfull

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*** YOU HAVE NEW MAIL ***

=> s nucleic acid

4 FILES SEARCHED...

343861 NUCLEIC ACID

=> s 11 and positiv? (3a) charge tag (3a) nucleic acid? 2 L1 AND POSITIV? (3A) CHARGE TAG (3A) NUCLEIC ACID?

=> d 12 bib abs 1-2

ANSWER 1 OF 2 WPIDS (C) 2002 THOMSON DERWENT L2

2002-674850 [72] AN WPIDS

CR 1997-393613 [36]

DNC C2002-190055

Composition useful for e.g. separation of nucleic acids comprises a ΤI positively or neutrally charged phosphoramidite.

DC B04 B05 D16

ALLAWI, H T; LYAMICHEV, V; NERI, B P; SKRZPCZYNSKI, Z; TAKOVA, T; WAYLAND, IN

(THIR-N) THIRD WAVE TECHNOLOGIES INC PΑ

CYC 100

PΙ WO 2002063030 A2 20020815 (200272)* EN 197p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM

zw

US 2002128465 A1 20020912 (200272)

ADT WO 2002063030 A2 WO 2002-US3423 20020206; US 2002128465 A1 CIP of US 1996-682853 19960712, CIP of US 1999-333145 19990614, US 2001-777430 20010206

FDT US 2002128465 A1 CIP of US 6001567

PRAI US 2001-777430 20010206; US 1996-682853 19960712; US 1999-333145

AN 2002-674850 [72] WPIDS

CR 1997-393613 [36]

AB WO 200263030 A UPAB: 20021108

NOVELTY - Composition comprises a positively or neutrally charged phosphoramidite.

DETAILED DESCRIPTION - Composition (c) or (c') comprises a positively charged phosphoramidite of formula (I) or a neutrally charged phosphoramidite of formula (II). (I) comprises nitrogen-containing chemical group selected from primary, secondary or tertiary amine or ammonium group. (II) comprises secondary or tertiary amine or ammonium group.

X, Z = a reactive phosphate group;

Y = a protected hydroxy group;

X' = a protected hydroxy group;

N, N' = an amine group.

INDEPENDENT CLAIMS are included for the following:

- (1) a composition (c1) comprising a charge tag (x1) attached to a terminal end of a **nucleic acid** molecule, the charge tag comprises a phosphate group and a positively charged molecule;
- (2) a composition (c2) comprising a nucleic acid molecule that comprises a positively charged phosphoramidite;
- (3) a composition (c3) comprising a charge tag attached to the terminal end of a nucleic acid molecule, the charge tag comprises a positively charged phosphoramidite;
- (4) a composition (c4) comprising a fluorescent dye directly bonded to a phosphate group, which is not directly bonded to an amine group;
- (5) a mixture (m) comprising a number of oligonucleotides, each oligonucleotide is attached to a different charge tag with each charge tag comprising a phosphate group and a positively charged group;
- (6) a composition (c5) comprising a solid support attached to a charged tag, the charge tag comprises a positively charged group and a reactive group configured to allow the charge tag to covalently attach to the nucleic acid molecule;
- (7) separating nucleic acid molecules involving either:
- (a) treating (ml) a charge-balanced oligonucleotide containing the charge tag to produce a charge-unbalanced oligonucleotide and separating the charge-unbalanced oligonucleotide from the reaction mixture; or
- (b) treating (m2) a number of charge-balanced oligonucleotides, each containing different charge tags, to produce at least 2 charge-unbalanced oligonucleotides, and separating the charge-unbalanced oligonucleotides from the reaction mixture.
- USE The composition is useful for separation of **nucleic** acid molecules (claimed). The composition is further useful for fractionation of specific nucleic acids by selective charge reversal useful in e.g. INVADER assay cleavage reactions; and in the synthesis of charge-balanced molecules.

ADVANTAGE - In the fractionation of **nucleic acid** molecules, the method provides an absolute readout of the partition of products from substrates (i.e. provides a 100% separation). Through the use of multiple positively charged adducts, synthetic molecules can be constructed with sufficient modification due to the fact that the normally negatively charged strand is made nearly neutral. It is also possible to distinguish between a enzymatically or thermally degraded DNA fragments

09567863

due to the absence or presence of 3'phosphate. Dwg.0/46

L2 ANSWER 2 OF 2 USPATFULL

AN 2002:236261 USPATFULL

TI Charge tags and the separation of nucleic acid molecules

IN Lyamichev, Victor, Madison, WI, UNITED STATES Skrzpczynski, Zbigniew, Verona, WI, UNITED STATES Allawi, Hatim T., Madison, WI, UNITED STATES Wayland, Sarah R., Madison, WI, UNITED STATES

Takova, Tsetska, Madison, WI, UNITED STATES Neri, Bruce P., Madison, WI, UNITED STATES

PA Third Wave Technologies, Inc. (U.S. corporation)

PI US 2002128465 Ā1 20020912

AI US 2001-777430 A1 20010206 (9)

RLI Continuation-in-part of Ser. No. US 1999-333145, filed on 14 Jun 1999, PENDING Continuation-in-part of Ser. No. US 1996-682853, filed on 12 Jul 1996, GRANTED, Pat. No. US 6001567

DT Utility

FS APPLICATION

LREP MEDLEN & CARROLL, LLP, 101 HOWARD STREET, SUITE 350, SAN FRANCISCO, CA, 94105

CLMN Number of Claims: 86 ECL Exemplary Claim: 1

DRWN 46 Drawing Page(s)

LN.CNT 5163

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention relates to novel phosphoramidites, including positive and neutrally charged compounds. The present invention also provides charge tags for attachment to materials including solid supports and nucleic acids, wherein the charge tags increase or decrease the net charge of the material. The present invention further provides methods for separating and characterizing molecules based on the charge differentials between modified and unmodified materials.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=>

=> d his (FILE 'HOME' ENTERED AT 10:12:59 ON 18 DEC 2002) FILE 'BIOSIS, MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 10:13:34 ON 18 DEC 2002 343861 S NUCLEIC ACID 1.1 2 S L1 AND POSITIV? (3A) CHARGE TAG (3A) NUCLEIC ACID? L2=> s l1 and positiv? (4a) charg? (3a) tag? 21 L1 AND POSITIV? (4A) CHARG? (3A) TAG? => s 13 not 12 19 L3 NOT L2 L4=> dup rem 15 L5 IS NOT VALID HERE The L-number entered has not been defined in this session, or it has been deleted. To see the L-numbers currently defined in this session, enter DISPLAY HISTORY at an arrow prompt (=>). => dup rem 14 PROCESSING COMPLETED FOR L4 19 DUP REM L4 (0 DUPLICATES REMOVED) => d 15 bib abs 1-19 ANSWER 1 OF 19 USPATFULL 2002:329813 USPATFULL AN Mutation analysis by mass spectrometry using photolytically cleavable TΤ Kostrzewa, Markus, Borsdorf-Panitzsch, GERMANY, FEDERAL REPUBLIC OF IN Frohlich, Thomas, Leipzig, GERMANY, FEDERAL REPUBLIC OF Wenzel, Thomas, Leipzig, GERMANY, FEDERAL REPUBLIC OF Jaschke, Andres, Berlin, GERMANY, FEDERAL REPUBLIC OF Hausch, Felix, Stanford, CA, UNITED STATES Bruker Saxonia Analytik GmbH, Leipzig, GERMANY, FEDERAL REPUBLIC OF PA (non-U.S. corporation) PΙ US 2002187493 A1 20021212 US 2002-79043 20020220 (10) **A1** AΙ DE 2001-108453 20010222 PRAI DTUtility FS APPLICATION KUDIRKA & JOBSE, LLP, ONE STATE STREET, SUITE 1510, BOSTON, MA, 02109 LREP Number of Claims: 22 CLMN ECL Exemplary Claim: 1 DRWN 2 Drawing Page(s) LN.CNT 708 The invention relates to a method of a mass-spectrometric analysis of AB known mutation sites in the genome, such as single nucleotide polymorphisms (SNPs), using the method of restricted primer extension. The invention consists of the use of primers with a photocleavable linker. The linker creates a gap in a DNA strand which is almost the

same size as a natural DNA building block (nucleoside). The linker forms a bridge over a base pair without inhibiting hybridization or enzymatic extension. However, the linker allows the primers to be cleaved after extension in order to obtain short DNA fragments which can be more

T₄5

easily detected on the mass spectrometer.

```
2002:322508 USPATFULL
       Enhanced secretion of a polypeptide by a microorganism
TТ
       Kolkman, Marc, Oegstgeest, NETHERLANDS
IN
PΙ
       US 2002182672
                         A1
                               20021205
       US 2001-975132
                          A1
                               20011009 (9)
ΑI
      US 2000-239531P
                          20001010 (60)
PRAI
DT
       Utility
      APPLICATION
FS
      VICTORIA L. BODY, GENENCOR INTERNATIONAL, INC., 925 PAGE MILL ROAD, PALO
LREP
       ALTO, CA, 94034-1013
CLMN
      Number of Claims: 52
ECL
      Exemplary Claim: 1
DRWN
       5 Drawing Page(s)
LN.CNT 1405
      Described herein are methods for the enhanced production of secreted
AΒ
       proteins. The secretion of a protein of interest having a substantially
      non-polar carboxy tail is enhanced by the placement of charged amino
       acid residues at the carboxy terminus either by adding to the native
       peptide or by replacing, i.e., substituting, the terminal residues of
       the native peptide.
     ANSWER 3 OF 19 USPATFULL
L_5
       2002:265886 USPATFULL
AN
       End selection in directed evolution
TТ
       Short, Jay M., Rancho Santa Fe, CA, UNITED STATES
IN
       Frey, Gerhard Johann, San Diego, CA, UNITED STATES
                               20021010
PΙ
       US 2002146762
                          Α1
                               20010619 (9)
       US 2001-885551
                          Α1
AΙ
       Continuation of Ser. No. US 2000-522289, filed on 9 Mar 2000, PATENTED
RLI
       Continuation-in-part of Ser. No. US 2000-498557, filed on 4 Feb 2000,
       PENDING Continuation-in-part of Ser. No. US 2000-495052, filed on 31 Jan
       2000, PENDING Continuation-in-part of Ser. No. US 1999-332835, filed on
       14 Jun 1999, ABANDONED Continuation-in-part of Ser. No. US 1999-276860,
       filed on 26 Mar 1999, PATENTED Continuation-in-part of Ser. No. US
       1999-267118, filed on 9 Mar 1999, PATENTED Continuation-in-part of Ser.
       No. US 1999-246178, filed on 4 Feb 1999, PATENTED Continuation-in-part
       of Ser. No. US 1998-185373, filed on 3 Nov 1998, PATENTED Continuation
       of Ser. No. US 1996-760489, filed on 5 Dec 1996, PATENTED
PRAI
       US 1995-8311P
                           19951207 (60)
DT
       Utility
FS
       APPLICATION
       GARY CARY WARE & FRIENDENRICH LLP, 4365 EXECUTIVE DRIVE, SUITE 1600, SAN
LREP
       DIEGO, CA, 92121-2189
CLMN
       Number of Claims: 4
ECL
       Exemplary Claim: 1
DRWN
       7 Drawing Page(s)
LN.CNT 8987
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       This invention provides methods of obtaining novel polynucleotides and
       encoded polypeptides by the use of non-stochastic methods of directed
       evolution (DirectEvolution.TM.). A particular advantage of
       end-selection-based methods is the ability to recover full-length
       polynucleotides from a library of progeny molecules generated by
       mutagenesis methods. These methods include non-stochastic polynucleotide
       site-saturation mutagenesis (Gene Site Saturation Mutagenesis.TM.) and
       non-stochastic polynucleotide reassembly (GeneReassembly.TM.). This
       invention provides methods of obtaining novel enzymes that have
       optimized physical &/or biological properties. Through use of the
       claimed methods, genetic vaccines, enzymes, small molecules, and other
       desirable molecules can be evolved towards desirable properties. For
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example, vaccine vectors, can be obtained that exhibit increased

efficacy for use as genetic vaccines. Vectors obtained by using the methods can have, for example, enhanced antigen expression, increased uptake into a cell, increased stability in a cell, ability to tailor an immune response, and the like. Furthermore, this invention provides methods of obtaining a variety of novel biologically active molecules, in the fields of antibiotics, pharmacotherapeutics, and transgenic traits.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

```
ANSWER 4 OF 19 USPATFULL
L_5
AN
       2002:265850 USPATFULL
ΤI
       Electrophoretic tag reagents comprising fluorescent compounds
       Matray, Tracy, San Lorenzo, CA, UNITED STATES
       Hernandez, Vincent, Brookdale, CA, UNITED STATES
       Singh, Sharat, San Jose, CA, UNITED STATES
       Aclara BioSciences, Inc. (U.S. corporation)
PA
PΙ
       US 2002146726
                          A1
                               20021010
                               20011109 (10)
AΙ
       US 2001-8495
                          A1
       Continuation-in-part of Ser. No. US 2000-698846, filed on 27 Oct 2000,
RLI
       PENDING Continuation-in-part of Ser. No. US 2000-602586, filed on 21 Jun
       2000, PENDING Continuation-in-part of Ser. No. US 2000-684386, filed on
       4 Oct 2000, PENDING Continuation-in-part of Ser. No. US 2000-561579,
       filed on 28 Apr 2000, ABANDONED Continuation-in-part of Ser. No. US
       1999-303029, filed on 30 Apr 1999, GRANTED, Pat. No. US 6322980
DT
       Utility
FS
       APPLICATION
       PERKINS COIE LLP, P.O. BOX 2168, MENLO PARK, CA, 94026
LREP
CLMN
       Number of Claims: 52
ECL
       Exemplary Claim: 1
       7 Drawing Page(s)
DRWN
LN.CNT 2991
```

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Electrophoretic probes comprising fluorescent compounds as detection groups and mobility modifiers are disclosed for the multiplexed detection of the binding of, or interaction between, one or more ligands and target antiligands are provided. In one embodiment, detection involves the release of identifying tags as a consequence of target recognition. Target antiligands are contacted with a set of e-tag probes and the contacted antiligands are treated with a selected cleaving agent resulting in a mixture of e-tag reporters. Typically, uncleaved or partially cleaved e-tag probes are removed and the mixture of e-tag reporters is separated by any technique that provides for separation by mass or mass to charge ratio and the like and detected to provide for target identification.

```
ANSWER 5 OF 19 USPATFULL
L5
       2002:258759 USPATFULL
AN
ΤI
       Compositions and methods employing cleavable electrophoretic tag
       reagents
       Matray, Tracy, San Lorenzo, CA, UNITED STATES
IN
       Hernandez, Vincent, Brookdale, CA, UNITED STATES
       Singh, Sharat, San Jose, CA, UNITED STATES
PΑ
       Aclara BioSciences, Inc. (U.S. corporation)
PΙ
       US 2002142329
                          A1
                               20021003
AΙ
       US 2001-8573
                          Al
                               20011109 (10)
       Continuation-in-part of Ser. No. US 2000-698846, filed on 27 Oct 2000,
RLI
       PENDING Continuation-in-part of Ser. No. US 2000-602586, filed on 21 Jun
       2000, PENDING Continuation-in-part of Ser. No. US 2000-684386, filed on
       4 Oct 2000, PENDING Continuation-in-part of Ser. No. US 2000-561579,
```

filed on 28 Apr 2000, ABANDONED Continuation-in-part of Ser. No. US 1999-303029, filed on 30 Apr 1999, GRANTED, Pat. No. US 6322980 DTUtility FS APPLICATION PERKINS COIE LLP, P.O. BOX 2168, MENLO PARK, CA, 94026 LREP Number of Claims: 71 CLMN Exemplary Claim: 1 ECL DRWN 9 Drawing Page(s) LN.CNT 3249 CAS INDEXING IS AVAILABLE FOR THIS PATENT. Probe sets for the multiplexed detection of the binding of, or AB interaction between, one or more ligands and target antiligands are provided. Detection involves the release of identifying tags as a consequence of target recognition. The probe sets include electrophoretic tag probes or e-tag probes, comprising a detection region and a mobility-defining region called the mobility modifier, both linked to a target-binding moiety. Target antiligands are contacted with a set of e-tag probes and the contacted antiligands are treated with a selected cleaving agent resulting in a mixture of e-tag reporters and uncleaved and/or partially cleaved e-tag probes. The mixture is exposed to a capture agent effective to bind to uncleaved or partially cleaved e-tag probes, followed by electrophoretic separation. In a multiplexed assay, different released e-tag reporters may be separated and detected providing for target identification. The methods employ compositions comprising luminescent molecules such as, for example, fluorescent molecules, which are modified to provide for electrophoretic properties that differ for each modified luminescent molecule while maintaining substantially the same absorption, emission and quantum yield properties of the original luminescent molecule. The compositions may be cleavably linked to binding molecules to form the e-tag probes. CAS INDEXING IS AVAILABLE FOR THIS PATENT. ANSWER 6 OF 19 USPATFULL L5 2002:243051 USPATFULL ANCompositions and methods for the therapy and diagnosis of ovarian cancer TIAlgate, Paul A., Issaquah, WA, UNITED STATES IN Jones, Robert, Seattle, WA, UNITED STATES Harlocker, Susan L., Seattle, WA, UNITED STATES Corixa Corporation, Seattle, WA, UNITED STATES, 98104 (U.S. corporation) PA US 2002132237 20020919 PΙ A1 ΑI US 2001-867701 A1 20010529 (9) US 2000-207484P 20000526 (60) PRAI DTUtility FS APPLICATION SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVE, SUITE 6300, LREP SEATTLE, WA, 98104-7092 CLMN Number of Claims: 11 ECLExemplary Claim: 1 DRWN No Drawings LN.CNT 25718 CAS INDEXING IS AVAILABLE FOR THIS PATENT. Compositions and methods for the therapy and diagnosis of cancer, ΆB particularly ovarian cancer, are disclosed. Illustrative compositions comprise one or more ovarian tumor polypeptides, immunogenic portions thereof, polynucleotides that encode such polypeptides, antigen presenting cell that expresses such polypeptides, and T cells that are

specific for cells expressing such polypeptides. The disclosed compositions are useful, for example, in the diagnosis, prevention

and/or treatment of diseases, particularly ovarian cancer.

```
ANSWER 7 OF 19 USPATFULL
L5
AN
       2002:171867 USPATFULL
ΤI
       Sets of generalized target-binding e-tag probes
       Singh, Sharat, San Jose, CA, UNITED STATES
IN
       Matray, Tracy, San Lorenzo, CA, UNITED STATES
       Chenna, Ahmed, Sunnyvale, CA, UNITED STATES
PI
       US 2002090616
                          A1
                                20020711
                                20010402 (9)
       US 2001-825244
                          A1
AΤ
       Continuation of Ser. No. US 1999-303029, filed on 30 Apr 1999, GRANTED,
RLI
       Pat. No. US 6322980 Continuation of Ser. No. US 2000-561579, filed on 28
       Apr 2000, ABANDONED Continuation of Ser. No. US 2000-602586, filed on 21
       Jun 2000, PENDING Continuation of Ser. No. US 2000-684386, filed on 4
       Oct 2000, PENDING Continuation of Ser. No. US 2000-698846, filed on 27
       Oct 2000, PENDING
       Utility
DT
       APPLICATION
FS
       PERKINS COIE LLP, P.O. BOX 2168, MENLO PARK, CA, 94026
LREP
CLMN
       Number of Claims: 20
       Exemplary Claim: 1
ECL
       45 Drawing Page(s)
DRWN
LN.CNT 4208
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Probe sets for the multiplexed detection of the binding of, or
       interaction between, one or more ligands and target antiligands are
       provided. Detection involves the release of identifying tags as a
       consequence of target recognition. The probe sets include
       electrophoretic tag probes or e-tag probes, comprising a detection
       region and a mobility-defining region called the mobility modifier, both
       linked to a target-binding moiety. Target antiligands are contacted with
       a set of e-tag probes and the contacted antiligands are treated with a
       selected cleaving agent resulting in a mixture of e-tag reporters and
       uncleaved and/or partially cleaved e-tag probes. The mixture is exposed
       to a capture agent effective to bind to uncleaved or partially cleaved
       e-tag probes, followed by electrophoretic separation. In a multiplexed
       assay, different released e-tag reporters may be separated and detected
       providing for target identification.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 8 OF 19 USPATFULL
L5
       2002:112528 USPATFULL
AN
       Generalized target-binding e-tag probe compositions
TI
       Singh, Sharat, San Jose, CA, UNITED STATES
Salimi-Moosavi, Hossein, Sunnyvale, CA, UNITED STATES
IN
       Xiao, Vivian, Cupertino, CA, UNITED STATES
PI
       US 2002058263
                          A1
                                20020516
AΙ
       US 2001-824861
                          Α1
                                20010402 (9)
       Continuation of Ser. No. US 1999-303029, filed on 30 Apr 1999, UNKNOWN
RLI
DT
       Utility
FS
       APPLICATION
       IOTA PI LAW GROUP, 350 CAMBRIDGE AVENUE SUITE 250, P O BOX 60850, PALO
LREP
       ALTO, CA, 94306-0850
       Number of Claims: 4
CLMN
ECL
       Exemplary Claim: 1
DRWN
       45 Drawing Page(s)
LN.CNT 4113
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB
       Compositions for the multiplexed detection of the binding of, or
       interaction between, one or more ligands and target antiligands are
       provided. The compositions include one or more uncleaved or partially
```

cleaved electrophoretic tag (e-tag) probes from a set of e-tag probes,

at least one e-tag reporter out of a possible set of e-tag reporters and a capture agent. Detection involves the release of identifying tags as a consequence of target recognition. The e-tag probes comprise a detection region and a mobility-defining region called the mobility modifier, both linked to a target-binding moiety. Target antiligands are contacted with a set of e-tag probes and the contacted antiligands are treated with a selected cleaving agent resulting in a mixture of e-tag reporters and uncleaved and/or partially cleaved e-tag probes. The mixture is exposed to a capture agent effective to bind to uncleaved or partially cleaved e-tag probes, followed by electrophoretic separation. In a multiplexed assay, different released e-tag reporters may be separated and detected providing for target identification.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

```
ANSWER 9 OF 19 USPATFULL
L5
AN
       2002:85692 USPATFULL
ΤI
       Oligonucleotide-binding e-tag probe compositions
TN
       Singh, Sharat, San Jose, CA, UNITED STATES
       Tian, Huan, Los Altos, CA, UNITED STATES
                               20020418
PΙ
       US 2002045738
                          A1
                               20010402 (9)
       US 2001-825245
                          A1
ΑI
       Continuation of Ser. No. US 1999-303029, filed on 30 Apr 1999, PENDING
RLI
       Continuation of Ser. No. US 2000-561579, filed on 28 Apr 2000, PENDING
       Continuation of Ser. No. US 2000-602586, filed on 21 Jun 2000, PENDING
       Continuation of Ser. No. US 2000-684386, filed on 4 Oct 2000, PENDING
       Continuation of Ser. No. US 2000-698846, filed on 27 Oct 2000, PENDING
DT
       Utility
       APPLICATION
FS
       IOTA PI LAW GROUP, 350 CAMBRIDGE AVENUE SUITE 250, P O BOX 60850, PALO
LREP
       ALTO, CA, 94306-0850
       Number of Claims: 19
CLMN
ECL
       Exemplary Claim: 1
DRWN
       45 Drawing Page(s)
LN.CNT 4184
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB
```

Compositions for the multiplexed detection of known, selected nucleotide target sequences are provided. The compositions include one or more uncleaved or partially cleaved electrophoretic tag (e-tag) probes from a set of e-tag probes, at least one e-tag reporter out of a possible set of e-tag reporters and a capture agent. The e-tag probes comprise a detection region and a mobility-defining region called the mobility modifier, both linked to a target-binding moiety. Detection involves the release of identifying tags as a consequence of target recognition. The target-binding moiety of the e-tag probes hybridizes to complementary target sequences followed by nuclease cleavage of the e-tag probes and release of detectable e-tags or e-tag reporters. The mixture is exposed to a capture agent which binds uncleaved and/or partially cleaved e-tag probes, followed by electrophoretic separation. In a multiplexed assay, different released e-tag reporters may be separated and detected providing for target identification.

```
ANSWER 10 OF 19 USPATFULL
L5
        2002:27108 USPATFULL
ΑN
        Sets of oligonucleotide-binding e-tag probes
TI
TN
        Singh, Sharat, San Jose, CA, UNITED STATES
        Matray, Tracy, San Lorenzo, CA, UNITED STATES
Chenna, Ahmed, Sunnyvale, CA, UNITED STATES
                                    20020207
PΙ
        US 2002015954
                             A1
        US 2001-825246
                                    20010402 (9)
AΙ
                              A1
```

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Continuation of Ser. No. US 1999-303029, filed on 30 Apr 1999, PENDING
RLI
       Continuation of Ser. No. US 2000-561579, filed on 28 Apr 2000, PENDING
       Continuation of Ser. No. US 2000-602586, filed on 21 Jun 2000, PENDING
       Continuation of Ser. No. US 2000-684386, filed on 4 Oct 2000, PENDING
       Continuation of Ser. No. US 2000-698846, filed on 27 Oct 2000, PENDING
DT
       Utility
FS
       APPLICATION
       IOTA PI LAW GROUP, 350 CAMBRIDGE AVENUE SUITE 250, P O BOX 60850, PALO
LREP
       ALTO, CA, 94306-0850
       Number of Claims: 15
CLMN
ECL
       Exemplary Claim: 1
DRWN
       45 Drawing Page(s)
LN.CNT 4140
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Probe sets for the multiplexed detection of known, selected nucleotide
       target sequences are provided. Detection involves the release of
       identifying tags as a consequence of target recognition. The probe sets
       include electrophoretic tag probes or "e-tag probes", comprising a
       detection region and a mobility-defining region called the mobility
       modifier, both linked to a target-binding moiety. The target-binding
       moiety of the e-tag probes hybridizes to complementary target sequences
       followed by nuclease cleavage of the e-tag probes and release of
       detectable e-tags or e-tag reporters. The mixture is exposed to a
       capture agent which binds uncleaved and/or partially cleaved e-tag
       probes, followed by electrophoretic separation. In a multiplexed assay,
       different released e-tag reporters may be separated and detected
       providing for target identification.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 11 OF 19 USPATFULL
L5
       2002:16857 USPATFULL
AN
       Kits employing oligonucleotide-binding e-tag probes
TI
       Singh, Sharat, San Jose, CA, UNITED STATES
IN
       Matray, Tracy, San Lorenzo, CA, UNITED STATES
       Chenna, Ahmed, Sunnyvale, CA, UNITED STATES
PΙ
       US 2002009737
                          A1
                               20020124
       US 2001-824905
                               20010402 (9)
AΙ
                          A1
       Continuation of Ser. No. US 1999-303029, filed on 30 Apr 1999, PENDING
RLI
       Continuation of Ser. No. US 2000-561579, filed on 28 Apr 2000, PENDING
       Continuation of Ser. No. US 2000-602586, filed on 21 Jun 2000, PENDING
       Continuation of Ser. No. US 2000-684386, filed on 4 Oct 2000, PENDING
       Continuation of Ser. No. US 2000-698846, filed on 27 Oct 2000, PENDING
DT
       Utility
FS
       APPLICATION
       Iota Pi Law Group, P.O. Box 60850, Palo Alto, CA, 94306-0850
LREP
CLMN
       Number of Claims: 10
ECL
       Exemplary Claim: 1
       45 Drawing Page(s)
DRWN
LN.CNT 4157
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Kits for the multiplexed detection of known, selected nucleotide target
       sequences are provided. Detection involves the release of identifying
       tags as a consequence of target recognition. The kits include sets of
       electrophoretic tag probes or e-tag probes, capture agent and optionally
       a nuclease. The e-tag probes comprise a detection region and a
       mobility-defining region called the mobility modifier, both linked to a
       target-binding moiety. In using the kits, the target-binding moiety of
       the e-tag probes hybridizes to complementary target sequences followed
       by nuclease cleavage of the e-tag probes and release of detectable
       e-tags or e-tag reporters. The mixture is exposed to a capture agent
       which binds uncleaved and/or partially cleaved e-tag probes, followed by
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electrophoretic separation. In a multiplexed assay, different released e-tag reporters may be separated and detected providing for target identification.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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ANSWER 12 OF 19 USPATFULL
       2002:3833 USPATFULL
AN
TI,
       Methods employing oligonucleotide-binding e-tag probes
       Singh, Sharat, San Jose, CA, UNITED STATES
IN
       Tian, Huan, Los Altos, CA, UNITED STATES
PΙ
       US 2002001808
                          A1
                               20020103
                               20010402 (9)
ΑI
       US 2001-825247
                          A1
       Continuation of Ser. No. US 1999-303029, filed on 30 Apr 1999, PENDING
RLI
       Continuation of Ser. No. US 2000-561579, filed on 28 Apr 2000, PENDING
       Continuation of Ser. No. US 2000-602586, filed on 21 Jun 2000, PENDING
       Continuation of Ser. No. US 2000-684386, filed on 4 Oct 2000, PENDING
       Continuation of Ser. No. US 2000-698846, filed on 27 Oct 2000, PENDING
DΤ
       Utility
       APPLICATION
FS
       IOTA PI LAW GROUP, 350 CAMBRIDGE AVENUE SUITE 250, P O BOX 60850, PALO
LREP
       ALTO, CA, 94306-0850
       Number of Claims: 10
CLMN
ECL
       Exemplary Claim: 1
       45 Drawing Page(s)
DRWN
LN.CNT 4155
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Methods for the multiplexed detection of known, selected nucleotide
       target sequences are provided. Detection involves the release of
```

Methods for the multiplexed detection of known, selected nucleotide target sequences are provided. Detection involves the release of identifying tags as a consequence of target recognition. The methods include the use of electrophoretic tag probes or e-tag probes, comprising a detection region and a mobility-defining region called the mobility modifier, both linked to a target-binding moiety. In practicing the methods, the target-binding moiety of the e-tag probes hybridizes to complementary target sequences followed by nuclease cleavage of the e-tag probes and release of detectable e-tags or e-tag reporters. The mixture is exposed to a capture agent which binds uncleaved and/or partially cleaved e-tag probes, followed by electrophoretic separation. In a multiplexed assay, different released e-tag reporters may be separated and detected providing for target identification.

```
L5
     ANSWER 13 OF 19 USPATFULL
AN
       2002:297432 USPATFULL
ΤI
       Non-stochastic generation of genetic vaccines
       Short, Jay M., Rancho Santa Fe, CA, United States
IN
       Diversa Corporation, San Diego, CA, United States (U.S. corporation)
PA
PΙ
       US 6479258
                            В1
                                  20021112
       US 2000-495052
AΙ
                                  20000131 (9)
       Continuation-in-part of Ser. No. US 1999-276860, filed on 26 Mar 1999 Continuation-in-part of Ser. No. US 1999-246178, filed on 4 Feb 1999,
RLI
       now patented, Pat. No. US 6171820 Continuation-in-part of Ser. No. US
       1998-185373, filed on 3 Nov 1998 Continuation-in-part of Ser. No. US
       1996-760489, filed on 5 Dec 1996, now patented, Pat. No. US 5830696
PRAI
       US 1995-8311P
                             19951207 (60)
DT
       Utility
FS
       GRANTED
       Primary Examiner: Park, Hankyel T.
EXNAM
LREP
       Gray Cary Ware & Freidenrich LLP, Haile, Lisa A.
CLMN
       Number of Claims: 86
ECL
       Exemplary Claim: 1
```

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LN.CNT 19213
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       This invention provides methods of obtaining vaccines by use of
       non-stochastic methods of directed evolution (DirectEvolution.TM.).
       These methods include non-stochastic polynucleotide site-satuaration
       mutagenesis (Gene Site Saturation Mutagenesis.TM.) and non-stochastic
       polynucleotide reassembly (GeneReassembly.TM.). Through use of the
       claimed methods, vectors can be obtained which exhibit increased
       efficacy for use as genetic vaccines. Vectors obtained by using the
       methods can have, for example, enhanced antigen expression, increased
       uptake into a cell, increased stability in a cell, ability to tailor an
       immune response, and the like.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 14 OF 19 USPATFULL
L5
AN
       2002:63712 USPATFULL
       Exonuclease-mediated nucleic acid reassembly in
TI
       directed evolution
       Short, Jay M., Rancho Santa Fe, CA, United States
TN
       Djavakhishvili, Tsotne David, San Diego, CA, United States
       Frey, Gerhard Johann, San Diego, CA, United States
PΑ
       Diversa Corporation, San Diego, CA, United States (U.S. corporation)
                               20020326
PΤ
       US 6361974
                          В1
       US 2000-535754
ΑI
                               20000327 (9)
       Continuation-in-part of Ser. No. US 2000-522289, filed on 9 Mar 2000
RLI
       Continuation-in-part of Ser. No. US 2000-498557, filed on 4 Feb 2000
       Continuation-in-part of Ser. No. US 2000-495052, filed on 31 Jan 2000
       Continuation-in-part of Ser. No. US 1999-332835, filed on 14 Jun 1999
       Continuation-in-part of Ser. No. US 1999-276860, filed on 26 Mar 1999
       Continuation-in-part of Ser. No. US 1999-267118, filed on 9 Mar 1999
       Continuation-in-part of Ser. No. US 1999-246178, filed on 4 Feb 1999
       Continuation-in-part of Ser. No. US 1998-185373, filed on 3 Nov 1998
       Continuation of Ser. No. US 1996-760489, filed on 5 Dec 1996, now
       patented, Pat. No. US 5830696 Continuation-in-part of Ser. No. US
       1997-962504, filed on 31 Oct 1997, now patented, Pat. No. US 6029056
       Continuation-in-part of Ser. No. US 1996-677112, filed on 9 Jul 1996,
       now patented, Pat. No. US 5965408 Continuation-in-part of Ser. No. US
       1996-651568, filed on 22 May 1996, now patented, Pat. No. US 5939250
PRAI
       US 1995-8311P
                           19951207 (60)
       US 1995-8316P
                           19951207 (60)
DT
       Utility
FS
       GRANTED
EXNAM
       Primary Examiner: Park, Hankyel T.
LREP
       Gray Cary Ware & Freidenrich, Haile, Lisa A., Shen, Greg
       Number of Claims: 15
CLMN
ECL
       Exemplary Claim: 1
DRWN
       6 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 7313
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       This invention provides methods of obtaining novel polynucleotides and
       encoded polypeptides by the use of non-stochastic methods of directed
       evolution (DirectEvolution.TM.). A particular advantage of
       exonuclease-mediated reassembly methods is the ability to reassemble
       nucleic acid strands that would otherwise be
       problematic to chimerize. Exonuclease-mediated reassembly methods can be
       used in combination with other mutagenesis methods provided herein.
       These methods include non-stochastic polynucleotide site-saturation
       mutagenesis (Gene Site Saturation Mutagenesis.TM.) and non-stochastic
       polynucleotide reassembly (GeneReassembly.TM.). This invention provides
       methods of obtaining novel enzymes that have optimized physical &/or
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66 Drawing Figure(s); 61 Drawing Page(s)

biological properties. Through use of the claimed methods, genetic vaccines, enzymes, small molecules, and other desirable molecules can be evolved towards desirable properties. For example, vaccine vectors can be obtained that exhibit increased efficacy for use as genetic vaccines. Vectors obtained by using the methods can have, for example, enhanced antigen expression, increased uptake into a cell, increased stability in a cell, ability to tailor an immune response, and the like. Furthermore, this invention provides methods of obtaining a variety of novel biologically active molecules, in the fields of antibiotics, pharmacotherapeutics, and transgenic traits.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L5
    ANSWER 15 OF 19 USPATFULL
       2002:57570 USPATFULL
AN
       End selection in directed evolution
TТ
       Short, Jay M., Encinitas, CA, United States
IN
       Frey, Gerhard Johann, San Diego, CA, United States
       Diversa Corporation, San Diego, CA, United States (U.S. corporation)
PA
       US 6358709
                               20020319
PΤ
                          B1
      US 2000-522289
                               20000309 (9)
AΤ
       Continuation-in-part of Ser. No. US 2000-498557, filed on 4 Feb 2000
RLI
       Continuation-in-part of Ser. No. US 2000-495052, filed on 13 Jan 2000
       Continuation-in-part of Ser. No. US 1999-332835, filed on 14 Jun 1999,
       now abandoned Continuation-in-part of Ser. No. US 1999-276860, filed on
       26 Mar 1999 Continuation-in-part of Ser. No. US 1999-267118, filed on 9
       Mar 1999, now patented, Pat. No. US 6238884 Continuation-in-part of Ser.
      No. US 1999-246178, filed on 4 Feb 1999, now patented, Pat. No. US
       6171820 Continuation-in-part of Ser. No. US 1998-185373, filed on 3 Nov
       1998 Continuation of Ser. No. US 1996-760489, filed on 5 Dec 1996, now
       patented, Pat. No. US 5830696 Continuation-in-part of Ser. No. US
       1997-962504, filed on 31 Oct 1997 Continuation-in-part of Ser. No. US
       1996-677112, filed on 9 Jul 1996, now patented, Pat. No. US 5965408
       Continuation-in-part of Ser. No. US 1996-651568, filed on 22 May 1996,
       now patented, Pat. No. US 5939250
PRAI
       US 1995-8311P
                           19951207 (60)
                           19951207 (60)
       US 1995-8316P
DT
       Utility
FS
       GRANTED
      Primary Examiner: Park, Hankyel T.
EXNAM
       Gray Cary Ware & Freidenrich LLP, Haile, Lisa A.
LREP
CLMN
       Number of Claims: 36
ECL
       Exemplary Claim: 1
       11 Drawing Figure(s); 7 Drawing Page(s)
DRWN
LN.CNT 7029
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       This invention provides methods of obtaining novel polynucleotides and
AB
       encoded polypeptides by the use of non-stochastic methods of directed
       evolution (DirectEvolution.TM.). A particular advantage of
       end-selection-based methods is the ability to recover full-length
       polynucleotides from a library of progeny molecules generated by
       mutagenesis methods. These methods include non-stochastic polynucleotide
       site-saturation mutagenesis (Gene Site Saturation Mutagenesis.TM.) and
       non-stochastic polynucleotide reassembly (GeneReassembly.TM.). This
       invention provides methods of obtaining novel enzymes that have
```

optimized physical &/or biological properties. Through use of the claimed methods, genetic vaccines, enzymes, small molecules, and other desirable molecules can be evolved towards desirable properties. For example, vaccine vectors can be obtained that exhibit increased efficacy for use as genetic vaccines. Vectors obtained by using the methods can have, for example, enhanced antigen expression, increased uptake into a

cell, increased stability in a cell, ability to tailor an immune

response, and the like. Furthermore, this invention provides methods of obtaining a variety of novel biologically active molecules, in the fields of antibiotics, pharmacotherapeutics, and transgenic traits.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

```
L5
     ANSWER 16 OF 19 USPATFULL
       2001:229389 USPATFULL
AN
       Kits employing generalized target-binding e-tag probes
TI
       Singh, Sharat, San Jose, CA, United States
TN
       Matray, Tracy, San Lorenzo, CA, United States
       Chenna, Ahmed, Sunnyvale, CA, United States
PΙ
       US 2001051340
                          A1
                               20011213
       US 2001-824851
                          A1
                               20010402 (9)
ΑI
       Continuation of Ser. No. US 1999-303029, filed on 30 Apr 1999, PENDING
RLI
       Continuation of Ser. No. US 2000-561579, filed on 28 Apr 2000, PENDING
       Continuation of Ser. No. US 2000-602586, filed on 21 Jun 2000, PENDING
       Continuation of Ser. No. US 2000-684386, filed on 4 Oct 2000, PENDING
       Continuation of Ser. No. US 2000-698846, filed on 27 Oct 2000, PENDING
DΥ
       Utility
       APPLICATION
FS
       IOTA PI LAW GROUP, 350 CAMBRIDGE AVENUE SUITE 250, P O BOX 60850, PALO
LREP
       ALTO, CA, 94306-0850
       Number of Claims: 4
CLMN
ECL
       Exemplary Claim: 1
       45 Drawing Page(s)
DRWN
LN.CNT 4110
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Kits for the multiplexed detection of the binding of, or interaction
AB
       between, one or more ligands and target antiligands are provided.
       Detection involves the release of identifying tags as a consequence of
       target recognition. The kits include sets of electrophoretic tag probes
       or e-tag probes, a capture agent and optionally a cleaving agent. The
       e-tag probes comprise a detection region and a mobility-defining region
       called the mobility modifier, both linked to a target-binding moiety. In
       using the kits, target antiligands are contacted with a set of e-tag
       probes and the contacted antiligands are treated with a selected
       cleaving agent resulting in a mixture of e-tag reporters and uncleaved
       and/or partially cleaved e-tag probes. The mixture is exposed to a
       capture agent effective to bind to uncleaved or partially cleaved e-tag
       probes, followed by electrophoretic separation. In a multiplexed assay,
       different released e-tag reporters may be separated and detected
       providing for target identification.
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ANSWER 17 OF 19 USPATFULL
L5
ΑN
       2001:223888 USPATFULL
       Methods employing generalized target-binding e-tag probes
TI
       Singh, Sharat, San Jose, CA, United States
IN
       Salimi-Moosavi, Hossein, Sunnyvale, CA, United States
       Xiao, Vivian, Cupertino, CA, United States
PΙ
       US 2001049105
                          A1
                               20011206
                               20010402 (9)
ΑI
       US 2001-824984
                          Α1
       Continuation of Ser. No. US 1999-303029, filed on 30 Apr 1999, PENDING
RLI
       Continuation of Ser. No. US 2000-561579, filed on 28 Apr 2000, PENDING
       Continuation of Ser. No. US 2000-602586, filed on 21 Jun 2000, PENDING
       Continuation of Ser. No. US 2000-684386, filed on 4 Oct 2000, PENDING
       Continuation of Ser. No. US 2000-698846, filed on 27 Oct 2000, PENDING
DT
       Utility
FS
       APPLICATION
       IOTA PI LAW GROUP, 350 CAMBRIDGE AVENUE SUITE 250, P O BOX 60850, PALO
LREP
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ALTO, CA, 94306-0850
      Number of Claims: 4
CLMN
       Exemplary Claim: 1
ECL
DRWN
       45 Drawing Page(s)
LN.CNT 4138
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Methods for the multiplexed detection of the binding of, or interaction
       between, one or more ligands and target antiligands are provided.
       Detection involves the release of identifying tags as a consequence of
       target recognition. The methods include the use of electrophoretic tag
       probes or e-tag probes, comprising a detection region and a
       mobility-defining region called the mobility modifier, both linked to a
       target-binding moiety. In practicing the methods, target antiligands are
       contacted with a set of e-tag probes and the contacted antiligands are
       treated with a selected cleaving agent resulting in a mixture of e-tag
       reporters and uncleaved and/or partially cleaved e-tag probes. The
       mixture is exposed to a capture agent effective to bind to uncleaved or
       partially cleaved e-tag probes, followed by electrophoretic separation.
       In a multiplexed assay, different released e-tag reporters may be
       separated and detected providing for target identification.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 18 OF 19 USPATFULL
L5
       2001:121236 USPATFULL
AN
       Method of nucleic acid analysis
TI
       Gut, Ivo G., Berlin, Germany, Federal Republic of
IN
       Beck, Stephan A., Cambridge, United Kingdom
       Imperial Cancer Research Technology Limited, London, United Kingdom
PA
       (non-U.S. corporation)
PΙ
       US 6268129
                               20010731
       WO 9627681 19960912
ΑI
       US 1997-894836
                               19971124 (8)
       WO 1996-GB476
                               19960304
                               19971124 PCT 371 date
                               19971124 PCT 102(e) date
PRAI
      GB 1995-4598
                           19950303
DT
      Utility
FS
       GRANTED
EXNAM Primary Examiner: Houtteman, Scott W.
LREP
      Nixon & Vanderhye P.C.
CLMN
      Number of Claims: 44
ECL
       Exemplary Claim: 1
DRWN
       31 Drawing Figure(s); 31 Drawing Page(s)
LN.CNT 1990
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       A method of analysing a nucleic acid by mass
AB
       spectrometry comprising the steps of: (1) preparing a nucleic
       acid molecule comprising a negatively charged non-phosphate
       sugar-sugar linkage; (2) eliminating the charge from all, or up to all
       but ten, of the sugar-sugar linkages of the said nucleic
       acid molecule; (3) introducing the said nucleic
       acid molecule in which the charge has been wholly or partly
       eliminated as said into a mass spectrometer; and (4) determining the
       mass of the said nucleic acid molecule. Preferably,
       the nucleic acid has no or one charge. A method of
       preparing a nucleic acid molecule containing no or
       up to ten negative charges and no or up to ten positive charges
       comprising the steps of (1) synthesizing a nucleic
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acid with a phosphorothioate linkage or a phosphoroselenoate linkage between sugar residues, and (2) reacting the said

nucleic acid with an alkylating agent so as to

eliminate the charge on the said phosphorothioate linkage or said phosphoroselenoate linkage. The methods are useful for DNA sequencing and mutation analysis, and the nucleic acids are useful to suppress gene expression. ##STR1##

CAS INDEXING IS AVAILABLE FOR THIS PATENT. ANSWER 19 OF 19 WPIDS (C) 2002 THOMSON DERWENT L52001-007201 [01] WPIDS AN 2002-075152 [10] CR DNC C2001-001816 Detecting a DNA sequence, particularly a single nucleotide polymorphism TT using a pair of nucleotide sequences, a primer and an snp detection sequence having an electrophoretic tag. DC B04 D16 SINGH, S; SALIMI-MOOSAVI, H; XIAO, V; CHENNA, A; MATRAY, T; TIAN, H IN (ACLA-N) ACLARA BIOSCIENCES INC; (SALI-I) SALIMI-MOOSAVI H; (SING-I) SINGH PA S; (XIAO-I) XIAO V; (CHEN-I) CHENNA A; (MATR-I) MATRAY T; (TIAN-I) TIAN H CYC 93 WO 2000066607 A1 20001109 (200101)* EN 76p PΙ RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW AU 2000044972 A 20001117 (200111) B1 20011127 (200175) US 6322980 US 2001049105 A1 20011206 (200203) US 2001051340 A1 20011213 (200204) US 2002001808 A1 20020103 (200207) US 2002009737 A1 20020124 (200210) US 2002015954 A1 20020207 (200213) A1 20020220 (200221) EN EP 1180112 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI US 2002045738 A1 20020418 (200228) US 2002058263 A1 20020516 (200237) US 2002090616 A1 20020711 (200248) WO 2000066607 A1 WO 2000-US11396 20000428; AU 2000044972 A AU 2000-44972 ADT20000428; US 6322980 B1 US 1999-303029 19990430; US 2001049105 A1 Cont of US 1999-303029 19990430, Cont of US 2000-561579 20000428, Cont of US 2000-602586 20000621, Cont of US 2000-684386 20001004, Cont of US 2000-698846 20001027, US 2001-824984 20010402; US 2001051340 A1 Cont of US 1999-303029 19990430, Cont of US 2000-561579 20000428, Cont of US 2000-602586 20000621, Cont of US 2000-684386 20001004, Cont of US 2000-698846 20001027, US 2001-824851 20010402; US 2002001808 A1 Cont of US 1999-303029 19990430, Cont of US 2000-561579 20000428, Cont of US 2000-602586 20000621, Cont of US 2000-684386 20001004, Cont of US 2000-698846 20001027, US 2001-825247 20010402; US 2002009737 A1 Cont of US 1999-303029 19990430, Cont of US 2000-561579 20000428, Cont of US 2000-602586 20000621, Cont of US 2000-684386 20001004, Cont of US 2000-698846 20001027, US 2001-824905 20010402; US 2002015954 A1 Cont of US 1999-303029 19990430, Cont of US 2000-561579 20000428, Cont of US 2000-602586 20000621, Cont of US 2000-684386 20001004, Cont of US 2000-698846 20001027, US 2001-825246 20010402; EP 1180112 A1 EP 2000-926444 20000428, WO 2000-US11396 20000428; US 2002045738 A1 Cont of US 1999-303029 19990430, Cont of US 2000-561579 20000428, Cont of US 2000-602586 20000621, Cont of US 2000-684386 20001004, Cont of US 2000-698846 20001027, US 2001-825245 20010402; US 2002058263 A1 Cont of US 1999-303029 19990430, US 2001-824861 20010402; US 2002090616 A1 Cont of US

1999-303029 19990430, Cont of US 2000-561579 20000428, Cont of US

2000-602586 20000621, Cont of US 2000-684386 20001004, Cont of US 2000-698846 20001027, US 2001-825244 20010402

FDT AU 2000044972 A Based on WO 200066607; EP 1180112 A1 Based on WO 200066607; US 2002090616 A1 Cont of US 6322980

PRAI US 1999-303029 19990430; US 2000-561579 20000428; US 2000-602586 20000621; US 2000-684386 20001004; US 2000-698846 20001027; US 2001-824984 20010402; US 2001-824851 20010402; US 2001-825247 20010402; US 2001-824905 20010402; US 2001-825246 20010402; US 2001-825244 20010402

AN 2001-007201 [01] WPIDS

CR 2002-075152 [10]

AB WO 200066607 A UPAB: 20020730

NOVELTY - DNA sequence in a target nucleic acid sample is detected by executing primer extension in the presence of a polymerase, target DNA (TA) and a reagent pair consisting of a primer which specifically binds to TA and detection sequence (DS) comprised of nucleotide bases for each DNA sequence to be determined that binds to TA downstream from primer and has an electrophoretic tag specific for each DNA sequence.

DETAILED DESCRIPTION - The above method (I) comprises:

- (a) combining under primer extension conditions, a polymerase having 5' to 3' exonuclease activity, TA and a reagent pair consisting of a primer and DS comprising of nucleotide bases for each DNA sequence to be determined, where each primer specifically binds to TA and DS binds to TA downstream from the primer in the direction of primer extension and has a electrophoretic tag specific for each DNA sequence;
- (b) executing at least 1 cycle of the primer extension, where DS bound to target DNA is at least partially degraded with release of the electrophoretic tag free of the detection sequence;
- (c) separating released electrophoretic tags into individual fractions; and
- (d) detecting the fractions using the tag, where the presence of the DNA sequence in the TA sample is detected, provided that, when separation is performed solely by differences in mass, the electrophoretic tags that are separated all have the same number of nucleotides bonded to the electrophoretic tag.

INDEPENDENT CLAIMS are also included for the following:

- (1) determining (II) the amount of at least 1 single nucleotide polymorphism (snp) in a target DNA sample, comprising:
- (a) combining with step (a) of (I), a quantitating system comprising at least 2 control sequences having a common primer region and different control detection regions downstream from the primer region in the direction of primer extension, a primer sequence complementary to the primer region and a control DS for each of the control detection regions characterized by having a labeled electrophoretic tag specific for the control DS to which it is bound;
- (b) executing at least 1 cycle of primer extension, where snp DS is bound to TA and control DS are partially degraded with release of electrophoretic tags;
- (c) electrophoretically separating the tags into separate bands and determining the signal from the label from each of the bands; and
- (d) comparing the band signal from control DS with signals from snp DS;
- (2) a kit comprising several snp detection sequences characterized by consisting of at least 12 nucleotides, the 5' nucleotide bonded to an electrophoretic tag, the penultimate nucleotide bonded to the adjacent nucleotide by a link resistant to exonuclease hydrolysis and a complementary nucleotide to a snp at other than the terminal nucleotide; and
- (3) a kit comprising several compounds of the formula: R-L-T, where R is a fluorescer, L is a linking group selected from NH-lysine,

NH-(lysine)2, NH-alanine, NH-aspartic acid, NH-(aspartic acid)2, NH-(aspartic acid)3, NH-(aspartic acid)4, NH-(aspartic acid)5, NH-(aspartic acid)6, NH-(aspartic acid)7, NH-alanine-lysine, NH-aspartic acid-lysine, NH-(aspartic acid)2-lysine, NH-(aspartic acid)3-lysine, NH-(aspartic acid)4-lysine, NH-(aspartic acid)5-lysine, NH-(aspartic acid) 6-lysine, NH-(aspartic acid) 7-lysine, NH-(aspartic acid) 8-lysine, NH-(lysine)4 and NH-(lysine)5 and T is selected from a purine, pyrimidine, nucleoside, nucleotide, and nucleotide triphosphate. USE - The method is useful for detecting at least 1 nucleic acid sequence or several snps in a target DNA sample. ADVANTAGE - The method provides an improved analysis of complex nucleic acid mixture and for simultaneous identification of several entities such as sequences, snps, alleles, mutations, etc. Dwg.0/9

=> d 15 18 kwic ANSWER 18 OF 19 USPATFULL TI Method of nucleic acid analysis A method of analysing a nucleic acid by mass AB spectrometry comprising the steps of: (1) preparing a nucleic acid molecule comprising a negatively charged non-phosphate sugar-sugar linkage; (2) eliminating the charge from all, or up to all but ten, of the sugar-sugar linkages of the said nucleic acid molecule; (3) introducing the said nucleic acid molecule in which the charge has been wholly or partly eliminated as said into a mass spectrometer; and (4) determining the mass of the said nucleic acid molecule. Preferably, the nucleic acid has no or one charge. A method of preparing a nucleic acid molecule containing no or up to ten negative charges and no or up to ten positive charges comprising the steps of (1) synthesizing a nucleic acid with a phosphorothicate linkage or a phosphoroselenoate linkage between sugar residues, and (2) reacting the said nucleic acid with an alkylating agent so as to eliminate the charge on the said phosphorothicate linkage or said phosphoroselenoate linkage. The. To date, a simple and effective method of making nucleic SUMM acid, particularly DNA, more suitable for analysis by mass spectroscopy, especially when the said nucleic acid has been enzymatically synthesised, has not been devised. A first aspect of the invention provides a method of analysing a SUMM nucleic acid by mass spectrometry comprising the steps of (1) providing a nucleic acid molecule containing no or up to ten negative charges and no or up to ten positive charges; (2) introducing the said nucleic acid molecule into a mass spectrometer; and (3) determining the mass of the said nucleic acid molecule, wherein when the nucleic acid molecule has no negative charges has greater than 17 sugar-sugar linkages and when the nucleic acid has a charge there are fewer charges than there are sugar-sugar linkages. Preferably, when the nucleic acid has no negative SUMM charges it has >20 sugar-sugar linkages; more preferably >30 sugar-sugar linkages; and still more preferably >50 sugar-sugar. SUMM A second aspect of the invention provides a method of analysing a nucleic acid by mass spectrometry comprising the steps of (1) preparing a nucleic acid molecule comprising a negatively charged non-phosphate sugar-sugar linkage; (2) eliminating

the charge from all, or up to all but ten, of the sugar-sugar linkages

of the said nucleic acid molecule; (3) introducing

- the said nucleic acid molecule in which the charge has been wholly or partly eliminated as said into a mass spectrometer; and (4) determining the mass of the said nucleic acid molecule.
- SUMM . . . molecule being analysed such as its relative, rather than its absolute, mass. Therefore, by "determining the mass of the said nucleic acid molecule" we include determination of any physical characteristic derivable from the mass or relative mass of the said nucleic acid molecule.
- SUMM It is preferred if the **nucleic acid** provided in the first aspect of the invention or prepared in the second aspect of the invention has no or. . .
- SUMM It is further preferred that the nucleic acid is DNA.
- SUMM . . . a diester with the said sugar residues. However, as will be clear from the specification we include in the term "nucleic acid" (and more particularly in the term DNA) molecules with non-phosphate linkages.
- SUMM By the term "nucleic acid" we also include molecules with non-natural base analogues; molecules in which the 2' and 3' positions of the pentose sugar. . .
- SUMM It is particularly preferred if the nucleic acid molecule has no phosphate sugar-sugar linkages.
- SUMM It is also preferred if the **nucleic acid** molecule has any of one to ten phosphate sugar-sugar linkages; most preferably one.
- SUMM Conveniently, when the nucleic acid is uncharged or positively charged, the mass is determined in positive ion mode (PIM); similarly, when the nucleic acid is negatively charged, the mass is determined in negative ion mode. Indeed, when the nucleic acid molecule is uncharged no signal is detected in NIM.
- SUMM The molecular masses of nucleic acid molecules as defined in the invention containing from two nucleoside moieties to around 1600 nucleoside moieties can be determined by mass spectroscopy and, as the spectrometers improve, it is envisaged that nucleic acid molecules of the invention of greater molecular mass could be used.
- SUMM It is most preferred if the **nucleic acid** molecule whose mass is determined has between 2 and 500 nucleoside moieties; preferably between 5 and 300 nucleoside moieties; and. . .
- SUMM Conveniently, the mass spectrometer is able to distinguish at least two nucleic acid molecules whose mass differs by the mass of a nucleoside moiety.
- SUMM Although in some circumstances it may be useful to determine the molecular mass of a single nucleic acid species, it is preferred that a plurality of nucleic acid molecules with differing molecular mass are introduced into the mass spectrometer and the mass of at least one of the. . .
- SUMM As will be discussed in more detail below, it is particularly preferred if the nucleic acid is prepared using an enzymatic chain extension step. It is particularly preferred if a polymerase chain reaction or a chain. . .
- SUMM The provision of a nucleic acid molecule containing no or up to ten negative and no or up to ten positive charges, and the preparation of a nucleic acid molecule comprising a negatively charged non-phosphate sugar-sugar linkage, as well as nucleic acid molecules which are suitable for use in the methods, are described in the following aspects of the invention.
- SUMM It is further preferred if certain salts are removed from the nucleic acid before introduction into the mass spectrometer. For example, NaI is produced in some of the methods

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described in the third aspect of the invention and it is convenient to
       remove this salt, and any buffer, from the nucleic
       acid. However, presence of NH.sub.4.sup.+ ions may increase the
       definition of the MS signal.
       It is still further preferred if the 5' end of any nucleic
SUMM
       acid is not a free hydroxyl. Preferably, as described below, it
      may be alkylated. It may also be phosphorylated (for example.
      A third aspect of the invention provides a method of preparing a
SUMM
      nucleic acid molecule containing no or up to ten
      negative charges and no or up to ten positive charges comprising the
       steps of (1) synthesising a nucleic acid with a
      phosphorothicate linkage or a phosphoroselenoate linkage between sugar
       residues, and (2) reacting the said nucleic acid
       with an alkylating agent so as to eliminate the charge on the said
      phosphorothicate linkage or said phosphoroselenoate linkage.
      A particular advantage of this method is that uncharged, or
SUMM
       substantially uncharged, nucleic acid can be made
      post-synthetically. A further advantage is that uncharged, or
       substantially uncharged, nucleic acid can be made
       which is longer than any uncharged nucleic acid that
      has been (or can be) made by de novo chemical synthesis.
      Preferably the nucleic acid is DNA. Conveniently the
SUMM
      nucleic acid molecule with a phosphorothicate linkage
       or with a phosphoroselenoate linkage is synthesised chemically, for
       example using solid phase phosphoramidite chemistry...
SUMM
       Alternatively, the nucleic acid molecule with a
      phosphorothicate linkage or with a phosphoroselencate linkage is
       synthesised enzymatically. In this embodiment, an .alpha.S-dNTP or an
       .alpha.Se-dNTP is incorporated into a growing nucleic
       acid chain using a polymerase enzyme. At least the
       .alpha.S-dNTPs are readily commercially available for example from
       United States Biochemical Corporation,.
SUMM
       The Klenow fragment of E. coli DNA polymerase is a preferred enzyme and
       in this embodiment a nucleic acid template and a
      primer are used to synthesise the nucleic acid
      molecule. Conveniently, the primer is an oligonucleotide wherein each of
       the sugar-sugar linkages is either a phosphorothicate or a
      phosphoroselenoate.
            . is preferred if step (1) of the method of the third aspect of
SUMM ·
       the invention further comprises (a) synthesising said nucleic
       acid with a taggable group, said taggable group being capable of
       accepting a positive charge either directly or indirectly either before
       or after step (2), or (b) synthesising said nucleic
       acid with a precursor that comprises a positively charged
      moiety.
      It is preferred if the taggable group accepts the
SUMM
      positive charge before step (2).
         . . or can be made positively charged. By "indirectly" we mean that
SUMM
       there is a linker (ie chemical spacer) between the taggable
      group and the positive charge.
SUMM
            . more detail in Example 5, amino (or ammonium) groups, more
      particularly quaternary ammonium tags, may usefully be added to the
      nucleic acid that is to be analysed by
      mass-spectrometry. Suitably, the amino (or ammonium) group is added to a
       synthetic oligonucleotide (such. . . positively charged group (which
       is preferably a quaternary ammonium-containing compound) is then
       attached to the aliphatic --NH.sub.2 group in the nucleic
       acid. Conveniently, the quaternary ammonium-containing compound
       comprises hydroxysuccinimidyl ester which reacts with aliphatic
       --NH.sub.2 groups; preferably the compound is trimethyl ammonium.
      The precursor of the nucleic acid may be any
SUMM
       suitable precursor which comprises a positively-charged moiety. It is
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particularly preferred if the precursor is a dideoxynucleotide comprising a positively charged moiety and that the precursor is introduced into the nucleic acid using a polymerase. Conveniently, the dideoxynucleotide comprising a positively charged moiety is made from a nucleotide precursor that comprises an aliphatic amino group. Suitably, the dideoxynucleotide comprising a positively charged moiety is introduced into the nucleic acid in a Sanger sequencing reaction.

- SUMM It is preferred if substantially all of the negative charges of the nucleic acid are removed and a single positive charge remains on the nucleic acid molecule.
- SUMM In one preferred embodiment, as well as an .alpha.S-dNTP or an .alpha.Se-dNTP being incorporated in a growing nucleic acid chain using a polymerase enzyme, a chain terminating a nucleotide is used in order to terminate the chain. Suitable chain.
- SUMM alpha.S-dNTP or .alpha.Se-dNTP (or a mixture thereof) in the presence of .alpha.S-ddNTP or .alpha.Se-ddNTP will lead to a plurality of nucleic acid molecules of varying sizes in which all of the sugar-sugar linkages are either a phosphorothioate linkage or a phosphoroselenoate linkage, . . . reacting with an alkylating agent so as to eliminate the charge on the said linkage. Thus, in this embodiment a nucleic acid molecule with no charge is produced.
- SUMM . . . has each sugar-sugar linkage as a phosphorothioate or phosphoroselenoate linkage, and either .alpha.S-dNTP or .alpha.Se-dNTP is used to extend the nucleic acid chain, then incorporation of a ddNTP will yield a nucleic acid molecule wherein the 3'-most sugar-sugar linkage is a phosphate linkage, and all other sugar-sugar linkages are either phosphorothioate or phosphoroselenoate.. . .
- SUMM . . . atom or phosphoroselenoate Se atom. Thus, it is preferred if the alkylating agent does not react with the bases of nucleic acid or with any free hydroxyl groups of the nucleic acid.
- SUMM . . . completely with the phosphorothicate S atom or phosphoroselencate Se atom and substantially completely with other reactive groups in the said nucleic acid, for example the bases of the nucleic acid or any free hydroxyl group of the nucleic acid.
- SUMM . . . case, it is preferred if the alkylating agent is substantially incapable of alkylating a phosphate group to form a stable nucleic acid.
- When the alkylated nucleic acid molecule of this third aspect of the invention is analysed using the first or second aspects of the invention it. . . Thus, it is particularly preferred that substantially all phosphorothicate linkages or substantially all phosphoroselenoate linkages of substantially all of the nucleic acid molecules are so alkylated. It does not matter if other reactive groups of the nucleic acid molecule (such as the bases or hydroxyl groups) so long as that alkylation is substantially complete and to the same. . .
- SUMM . . . is important so that the masses or mass differences detected reflect differences in the number of nucleoside moieties in a nucleic acid molecule rather than the extent of alkylation.
- SUMM . . . more detail in the Examples, the mass of each (or at least a substantial number) of the plurality of the nucleic acid molecules so generated can be determined according to the first or second aspect of the invention and, because the mass. . difference expected for each nucleoside moiety (comprising a base A, G, C or T) is known, the sequence of a nucleic acid can

be determined.

- SUMM . . . the invention) can be used to determine mutations in a DNA sequence. Thus, for example, the mass of a given nucleic acid sequence can be readily calculated from the known molecular masses of bases, sugar and sugar-sugar linkages. If one or more bases is replaced by another base (as occurs in a mutation), the mass of the said given nucleic acid sequence will change in a predictable way. Thus, as is apparent (and is described in more details in the Examples). . .
- SUMM In this embodiment of the invention it is particularly preferred if the nucleic acid molecule with a given sequence is produced by a polymerase chain reaction. The primers used in the PCR may be. . .
- SUMM . . . the primers contain no phosphate linkage. The sequence of the primers are designed using well established principles so that the nucleic acid sequence of interest is amplified.

 Conveniently, .alpha.S-dNTPs or .alpha.Se-dNTPs are used and the resulting DNA molecule has only either phosphorothioate. . .
- SUMM A fourth aspect of the invention provides a method of preparing a nucleic acid molecule containing no or up to ten negative charges comprising the steps of synthesising enzymatically the said nucleic acid using a dNTP uncharged at least at the .alpha.-phosphorus position.
- SUMM Conveniently, the nucleic acid is synthesised using a primer and a polymerase.
- SUMM As described in relation to the third aspect of the invention, various nucleic acid molecules are suitable as primers. It is preferred if the primer is an oligonucleotide wherein each of the sugar-sugar linkages. . .
- SUMM A fifth aspect of the invention provides an uncharged nucleic acid molecule has greater than 17 sugar-sugar linkages.

 Preferably, the nucleic acid molecule has >20; more preferably >30 and still more preferably >50 sugar-sugar linkages. Such molecules are readily synthesised using, for. . .
- SUMM A sixth aspect of the invention provides a nucleic acid molecule with no or up to ten negative charges wherein at least one sugar-sugar linkage comprises an alkylated phosphorothicate moiety. . .
- SUMM A seventh aspect of the invention provides an uncharged **nucleic**acid molecule comprising a phosphoro sugar-sugar linkage wherein

 in each phosphoro linkage the phosphorous atom is substituted with any
 one of. . .
- An eighth aspect of the invention provides a nucleic acid molecule containing one to ten phosphate sugar-sugar linkages wherein all other sugar-sugar linkages are uncharged.

 Preferably the nucleic acid comprises at least 20 nucleoside residues; more preferably at least 50 nucleoside residues.
- SUMM A further aspect of the invention provides a nucleic acid with one or up to ten positive charges wherein the sugar-sugar linkages are uncharged. Preferably, each sugar-sugar linkage is either an, alkylated phosphorothioate moiety or an alkylated phosphoroselenoate moiety. More preferably the nucleic acid has a single positive charge. The nucleic acids of this aspect of the invention can be synthesised using a method. . .
- SUMM . . . completely with the phosphorothicate S atom or phosphoroselenoate Se atom and substantially completely with other reactive groups in the said nucleic acid molecule.
- SUMM Preferably the use to which the alkylating agent is put is to alkylate a nucleic acid wherein each of the sugar-sugar linkages is either a phosphorothicate or a phosphoroselencate linkage; or wherein up to ten sugar-sugar. . .
- SUMM . . . of the invention provide a method of suppressing gene

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expression in a cell comprising administering to the cell an antisense
nucleic acid wherein the antisense nucleic
acid is a nucleic acid obtainable by the
third and fourth aspects of the invention or a nucleic
acid of the fifth, sixth, seventh or eighth aspects of the
invention; use of any of the said nucleic acids as an antisense
nucleic acid; a said nucleic acid
for use in medicine; and a pharmaceutical formulation comprising a said
nucleic acid and a pharmaceutically acceptable
carrier.
It is particularly preferred that the nucleic acid
is the nucleic acid obtainable by the method of the
third aspect of the invention, in particular by synthesising a
nucleic acid with a phosphorothicate linkage between
sugar residues and reacting the said nucleic acid
with an alkylating agent so as to eliminate the charge on the said
phosphorothioate linkage.
      . (more usually referred to as antisense oligonucleotides
although we do not use this to indicate a size limitation) are
single-stranded nucleic acid, which can specifically
bind to a complementary nucleic acid sequence. By
binding to the appropriate target sequence, an RNA-RNA, a DNA-DNA, or
RNA-DNA duplex is formed. These nucleic acids.
                                                . . could recognise
sequences in the major groove of the DNA double helix. A triple helix
was formed thereby. Thus, the nucleic acid molecules
of the invention may be able to specifically bind double-stranded DNA
via recognition of major groove hydrogen binding sites.
By binding to the target nucleic acid, the above
oligonucleotides can inhibit the function of the target nucleic
acid. This is, for example, a result of blocking the
 transcription, processing, poly(A) addition. replication, translation,
or promoting inhibitory mechanisms of.
   . . HL60, which over expresses the c-myc proto-oncogene. The
antisense oligonucleotide used was complementary to regions of the c-myc
mRNA. A nucleic acid of the present invention with
the same base sequence is expected to work in the same way with an
advantage.
Antisense oligonucleotides can also be used to inhibit replication and
expression of nucleic acid foreign to the host
cells. The antisense oligonucleotides are prepared as described above
and then introduced into cells, for example.
   . . amount. The local high concentration of oligonucleotides
enhances penetration of the targeted cells and effectively blocks
translation of the target nucleic acid sequences.
A still further aspect of the invention provides a method of analysing a
nucleic acid by mass spectrometry comprising the steps
of (1) providing a nucleic acid molecule comprising
a positively-charged moiety; (2) introducing the said nucleic
acid molecule into a mass spectrometer; and (3) determining the
mass of the said nucleic acid. Preferably the
sugar-sugar linkages of the nucleic acid are
substantially all phosphate sugar-sugar linkages. As is shown in Example
 5, there are advantages to including a positively charged moiety into a
nucleic acid whether or not the negative charges of
the sugar-sugar linkages are eliminated or not.
A further aspect of the invention provides a method of preparing a
nucleic acid comprising a positively-charged moiety
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comprising synthesising a nucleic acid with a

sugar-sugar linkages of the nucleic acid are substantially all phosphate sugar-sugar linkages.

taggable group, said taggable group being capable of accepting a positive charge either directly or indirectly. Preferably, the

DETD

SUMM . . . or can be made positively charged. By "indirectly" we mean that there is a linker (ie chemical spacer) between the **taggable** group and the **positive charge**.

SUMM . . . more detail in Example 5, amino (or ammonium) groups, more particularly quaternary ammonium tags, may usefully be added to the

nucleic acid that is to be analysed by mass-spectrometry. Suitably, the amino (or ammonium) group is added to a synthetic oligonucleotide (such. . . positively charged group (which is preferably a quaternary ammonium-containing compound) is then attached to the aliphatic --NH.sub.2 group in the nucleic acid. Conveniently, the quaternary ammonium-containing compound comprises hydroxysuccinimidyl ester which reacts with aliphatic --NH.sub.2 groups: preferably the compound is trimethyl ammonium. . .

--NH.sub.2 groups; preferably the compound is trimethyl ammonium. . . . efficient and clean. The combination of these two reactions is very simple. No side products were observed. Attaching a single positive charge via a charge tag

has the advantage that there is no need for a high acidity in the matrix which leads to degradation of. . .

CLM What is claimed is:

- 1. A method of analyzing a nucleic acid by mass spectrometry comprising the steps of (1) providing a positively charged or negatively charged nucleic acid molecule containing one or up to ten negative charges and no or up to ten positive charges, or no negative charges and one or up to ten positive charges, wherein the nucleic acid molecule has a sugar-linkage-sugar backbone and said sugars have a base attached thereto at the 1 position; and there are fewer negative charges than there are sugar-sugar linkages; (2) introducing the said nucleic acid molecule into a mass spectrometer; and (3) determining the mass of the said nucleic acid molecule.
- 2. A method of analyzing a nucleic acid by mass spectrometry wherein the nucleic acid molecule has a sugar-linkage-sugar backbone and said sugars have a base attached thereto at the 1 position; said method comprising the steps of (1) preparing a nucleic acid molecule comprising a negatively charged non-phosphate sugar-sugar linkage; (2) eliminating charge from the sugar-sugar linkages of the said nucleic acid molecule by covalent modification of the negatively charged non-phosphate sugar-sugar linkage so that the resulting nucleic acid molecule is positively charged or negatively charged and said molecule contains one or up to ten negative charges, being fewer charges than there are sugar-sugar linkages; (3) introducing the said nucleic acid molecule in which the charge has been partly eliminated as said into a mass spectrometer; and (4) determining the mass of the said nucleic acid molecule.
- 3. A method according to claim 2 wherein the said nucleic acid molecule has one phosphate sugar-sugar linkage.
- 4. A method according to claim 1 wherein the nucleic acid has one charge.
- 5. A method according to claim 1 wherein the **nucleic** acid DNA or an analouge or derivative thereof wherein the sugar residue comprises a 2'-deoxyribose.
- 7. A method according to claim 1 wherein when the **nucleic** acid is uncharged or positively charged the mass is determined by detection in positive ion mode.
- 8. A method according to claim 1 wherein when the nucleic

acid is negatively charged the mass is determined by detection in negative ion mode.

- 9. A method according to claim 1 wherein a plurality of nucleic acid molecules with differing molecular mass are introduced into the mass spectrometer and the mass of at least one of the. 10. A method according to claim 1 wherein an enzymatic chain extension step is used in the preparation of the nucleic acid.
- . A method according to claim 9 wherein a polymerase chain reaction is used in the preparation of the plurality of nucleic acid molecules.
 - 12. A method according to claim 9 wherein a **nucleic** acid chain terminating reagent is used in the preparation of the plurality of nucleic acids.
 - . step of determining a nucleotide sequence or detecting a mutation by comparing the mass differences of the said plurality of nucleic acid molecules.
 - 14. A method of preparing a nucleic acid molecule containing no or up to ten negative charges or a nucleic acid molecule containing no or up to ten positive charges wherein the nucleic acid molecule has a sugar-linkage-sugar backbone and said sugars have a base attached thereto at the 1 position; said method comprising the steps of (1) synthesizing a nucleic acid with a phosphorothicate linkage or a phosphoroselenoate linkage between sugar residues, and (2) reacting the said nucleic acid with an alkylating agent so as to eliminate the charge on the said phosphorothicate linkage or said phosphoroselenoate linkage wherein step (1) further comprises (a) synthesizing said nucleic acid with a taggable group, said taggable group being capable of accepting a positive charge either directly or indirectly and either before or after step (2), or (b) synthesizing said nucleic acid with a precursor that comprises a positively charged moiety.
 - 15. A method of preparing a positively charged or negatively charged nucleic acid molecule containing one or up to ten negative charges and no or up to ten positive charges or no negative charges and one or up to ten positive charges, said nucleic acid molecule comprising a sugar-linkage-sugar backbone wherein said sugars have a base attached thereto at the 1 position; said method comprising the steps of (1) enzymatically synthesizing a nucleic acid with a phosphorothicate linkage or a phosphoroselencate linkage between sugar residues, and (2) reacting the said nucleic acid with an alkylating agent so as to eliminate the charge on the said phosphorothicate linkage or said phosphoroselencate linkage, wherein said nucleic acid molecule consists of at least 4 nucleoside moieties.
 - 16. A method of analyzing a nucleic acid by mass spectrometry comprising the steps of (1) providing a positively or negatively charged nucleic acid molecule obtainable by the method of claim 15, containing one or up to ten negative charges and no or up. . . up to ten positive charges, wherein there are fewer negative charges than there are sugar-sugar linkages; (2) introducing the said nucleic acid molecule into a mass spectrometer; and (3) determining the mass of the said nucleic acid molecule.

- 17. A method according to claim 14 wherein the **nucleic** acid with a phosphorothicate linkage or a phosphoroselenoate linkage is synthesized chemically.
- 18. A method according to claim 14 wherein the nucleic acid is synthesized by copying a nucleic acid template using a primer, a polymerase and dNTP-.alpha.-S or dNTP-.alpha.-Se.
- 25. A method of preparing a nucleic acid molecule containing no or up to ten negative charges or a nucleic acid molecule containing no or up to ten positive charges wherein the nucleic acid molecule has a sugar-linkage-sugar backbone and said sugars have a base attached thereto at the 1 position; said method comprising the steps of (1) synthesizing a nucleic acid with a phosphorothicate linkage or a phosphoroselenoate linkage between sugar residues, and (2) reacting the said nucleic acid with an alkylating agent so as to eliminate the charge on the said phosphorothicate linkage or said phosphoroselenoate linkage, wherein the nucleic acid chain is synthesized enzymatically and is terminated using a ddNTP, a ddNTP-.alpha.-S or a ddNTP-.alpha.-Se.
- . completely with the phosphorothicate S atom or phosphoroselenoate Se atom and substantially completely with other reactive groups in the said nucleic acid.
- 32. A method of preparing a nucleic acid molecule containing one or up to ten negative charges wherein the nucleic acid molecule has a sugar-linkage-sugar backbone and said sugars have a base attached thereto at the 1 position; said method comprising the steps of synthesizing enzymatically the said nucleic acid using a dNTP uncharged at least at the .alpha.-phosphorus position, wherein the nucleic acid is synthesized additionally using a primer and a polymerase and wherein the said dNTP uncharged at least at the .alpha.-phosphorus position is enzymatically incorporated into the said nucleic acid molecule.
- 38. A nucleic acid molecule comprising a sugar-linkage-sugar backbone wherein said sugars have a base attached thereto at the 1 position; said molecule further. . . . 39. A nucleic acid according to claim 38 comprising at least 50 nucleoside residues.
- 40. A nucleic acid with one or up to ten positive charges wherein the sugar-sugar linkages are uncharged.
- 41. A **nucleic acid** according to claim 40 wherein each sugar-sugar linkage is either an alkylated phosphorothicate moiety or an alkylated phosphoroselenoate moiety.
- 42. A method of analyzing a nucleic acid by mass spectrometry comprising the steps of (1) preparing a nucleic acid according to the method of claim 14; (2) introducing the said nucleic acid molecule into a mass spectrometer; and (3) determining the mass of the said nucleic acid
- 43. A method according to claim 42 wherein the sugar-sugar linkages of the **nucleic acid** are substantially all phosphate sugar-sugar linkages.

44. A method according to claim 1, wherein said nucleic acid molecule comprises a non-phosphate sugar-sugar linkage.

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=> s positiv? (3a) charq? (3a) label? (4a) terminal (4a) (nucleic acid? or oligo? 4 FILES SEARCHED... 1 POSITIV? (3A) CHARG? (3A) LABEL? (4A) TERMINAL (4A) (NUCLEIC ACID? OR OLIGO? OR DNA) => d l11 bib abs kwic L11 ANSWER 1 OF 1 USPATFULL 2002:243051 USPATFULL AN Compositions and methods for the therapy and diagnosis of ovarian cancer ΤI Algate, Paul A., Issaquah, WA, UNITED STATES IN Jones, Robert, Seattle, WA, UNITED STATES Harlocker, Susan L., Seattle, WA, UNITED STATES Corixa Corporation, Seattle, WA, UNITED STATES, 98104 (U.S. corporation) PA US 2002132237 20020919 PΤ **A1** ΑI US 2001-867701 **A1** 20010529 (9) PRAI US 2000-207484P 20000526 (60) Utility DT APPLICATION FS SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVE, SUITE 6300, LREP SEATTLE, WA, 98104-7092 Number of Claims: 11 CLMN ECL Exemplary Claim: 1 No Drawings DRWN LN.CNT 25718 CAS INDEXING IS AVAILABLE FOR THIS PATENT. Compositions and methods for the therapy and diagnosis of cancer, AB particularly ovarian cancer, are disclosed. Illustrative compositions comprise one or more ovarian tumor polypeptides, immunogenic portions thereof, polynucleotides that encode such polypeptides, antigen

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM [2043] SEQ ID NO: 2004 represents the cDNA sequence for clone AA165409.

specific for cells expressing such polypeptides. The disclosed compositions are useful, for example, in the diagnosis, prevention

and/or treatment of diseases, particularly ovarian cancer.

presenting cell that expresses such polypeptides, and T cells that are

TN

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=> s mass tag
          110 MASS TAG
L13
=> s 113 and oligonucleotide?
            50 L13 AND OLIGONUCLEOTIDE?
=> s 114 and label?
           43 L14 AND LABEL?
L15
=> s l15 and terminal
           21 L15 AND TERMINAL
L16
=> dup rem 116
PROCESSING COMPLETED FOR L16
             21 DUP REM L16 (0 DUPLICATES REMOVED)
=> d l17 bib abs 1-21
L17 ANSWER 1 OF 21 USPATFULL
       2002:322488 USPATFULL
AN
TΙ
       Proteomic analysis
       Cravatt, Benjamin F., La Jolla, CA, UNITED STATES
IN
       Sorensen, Erik, San Diego, CA, UNITED STATES
       Patricelli, Matthew P., San Diego, CA, UNITED STATES
       Lovato, Martha, San Diego, CA, UNITED STATES
       Adam, Gregory, San Diego, CA, UNITED STATES
PΙ
       US 2002182652
                          A1
                               20021205
       US 2002-158498
                               20020529 (10)
ΑI
                          A1
      Division of Ser. No. US 2000-738954, filed on 15 Dec 2000, PENDING
RLI
      US 2000-195954P
                           20000410 (60)
PRAI
      US 2000-212891P
                           20000620 (60)
       US 2000-222532P
                           20000802 (60)
DT
      Utility
FS
       APPLICATION
       GARY CARY WARE & FRIENDENRICH LLP, 4365 EXECUTIVE DRIVE, SUITE 1600, SAN
LREP
      DIEGO, CA, 92121-2189
CLMN
      Number of Claims: 14
ECL
      Exemplary Claim: 1
DRWN
       24 Drawing Page(s)
LN.CNT 3576
       The present invention provides methods for analyzing proteomes, as cells
AB
       or lysates. The analysis is based on the use of probes that have
       specificity to the active form of proteins, particularly enzymes and
       receptors. The probes can be identified in different ways. In accordance
       with the present invention, a method is provided for generating and
       screening compound libraries that are used for the identification of
       lead molecules, and for the parallel identification of their biological
       targets. By appending specific functionalities and/or groups to one or
       more binding moieties, the reactive functionalities gain binding
       affinity and specificity for particular proteins and classes of
       proteins. Such libraries of candidate compounds, referred to herein as
       activity-based probes, or ABPs, are used to screen for one or more
       desired biological activities or target proteins.
L17 ANSWER 2 OF 21 USPATFULL
AN
       2002:322437 USPATFULL
       Method and reagents for analyzing the nucleotide sequence of nucleic
ΤI
```

Sampson, Jeffrey R., Burlingame, CA, UNITED STATES

Myerson, Joel, Berkeley, CA, UNITED STATES

Tsalenko, Anna M., Chicago, IL, UNITED STATES Sampas, Nicholas M., San Jose, CA, UNITED STATES Webb, Peter G., Menlo Park, CA, UNITED STATES Yakhini, Zohar H., Zikhron Ya'Acov, ISRAEL A1 20021205 PΤ US 2002182601 US 2001-836012 20010417 (9) ΑI Α1 Continuation-in-part of Ser. No. US 1998-112437, filed on 9 Jul 1998, RLI GRANTED, Pat. No. US 6218118 DT Utility FS APPLICATION AGILENT TECHNOLOGIES, Legal Department, DL429, Intellectual Property LREP Administration, P.O. Box 58043, Santa Clara, CA, 95052-8043 CLMN Number of Claims: 80 Exemplary Claim: 1 ECL 13 Drawing Page(s) DRWN LN.CNT 3253 Methods and reagents are disclosed which provide for more sensitive, AB more accurate and higher through-put analyses of target nucleic acid sequences. The methods and reagents of the present invention may be generically applied to generally any target nucleic acid sequence and do not require a priori information about the presence, location or identity of mutations in the target nucleic acid sequence. The reagents of the invention are mixtures of oligonucleotide precursors having a high level of coverage and mass number complexity, and also having tags analyzable by mass spectrometry which are covalently linked to the precursors through cleavable bonds. A method is also disclosed for analyzing a target nucleic acid sequence employing the mixtures of oligonucleotide precursors having tags analyzable by mass spectrometry covalently linked to the oligonucleotide precursors through cleavable bonds, and chemical or enzymatic assays to alter the mass of the oligonucleotide precursors prior to mass spectral analysis. The enzymatic assay may be a polymerase extension assay or a ligation-based assay. The kits for carrying out the methods of the invention are also disclosed. L17 ANSWER 3 OF 21 USPATFULL 2002:307838 USPATFULL AN Mass defect labeling for the determination of oligomer ΤI sequences Schneider, Luke V., Half Moon Bay, CA, UNITED STATES TN Hall, Michael P., San Carlos, CA, UNITED STATES Petesch, Robert, Newark, CA, UNITED STATES Target Discovery, San Carlos, CA, UNITED STATES, 94070 (U.S. PAcorporation) PΙ US 2002172961 20021121 A1 ΑI US 2001-35349 **A**1 20011019 (10) US 2000-242165P 20001019 (60) PRAI US 2000-242398P 20001019 (60) DT Utility APPLICATION FS LREP TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH FLOOR, SAN FRANCISCO, CA, 94111-3834 CLMN Number of Claims: 50 ECL Exemplary Claim: 1 32 Drawing Page(s) LN.CNT 3568 CAS INDEXING IS AVAILABLE FOR THIS PATENT. AΒ Mass tagging methods are provided that lead to mass spectrometer detection sensitivities and molecular discriminations that are improved over other methods. In particular the methods are useful for

discriminating tagged molecules and fragments of molecules from chemical

noise in the mass spectrum. These mass tagging methods are useful for oligomer sequencing, determining the relative abundances of molecules from different samples, and identifying individual molecules or chemical processing steps in combinatorial chemical libraries. The methods provided are useful for the simultaneous analysis of multiple molecules and reaction mixtures by mass spectrometric methods.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L17 ANSWER 4 OF 21 USPATFULL
       2002:301101 USPATFULL
AΝ
ΤI
       Methods for isolation and labeling of sample molecules
       Aebersold, Rudolf H., Mercer Island, WA, UNITED STATES
IN
       Zhou, Huilin, Seattle, WA, UNITED STATES
       US 2002168644
                               20021114
DΤ
                          A1
       US 2001-858198
                               20010514 (9)
                          A1
ΑI
       Utility
DΤ
       APPLICATION
FS
LREP
       CAMPBELL & FLORES LLP, 4370 LA JOLLA VILLAGE DRIVE, 7TH FLOOR, SAN
       DIEGO, CA, 92122
       Number of Claims: 105
CLMN
ECL
       Exemplary Claim: 1
       13 Drawing Page(s)
DRWN
LN.CNT 1592
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The invention provides methods for labeling a molecule by
       contacting a sample molecule with a solid support coupled to a chemical
       group comprising a cleavable functional group, one or more functional
       groups, and a reactive group for the sample molecule, under conditions
       allowing the sample molecule to covalently bind to the reactive group;
       and cleaving the cleavable functional group, thereby releasing the
       sample molecule comprising the one or more functional groups, which can
       be a tag. The invention also provides a solid support covalently coupled
       to a chemical group comprising a cleavable functional group, a mass
       spectrometry tag and a reactive group for covalently attaching a sample
       molecule, wherein the cleavable functional group, the tag and the
       reactive group are positioned relative to each other to allow transfer
       of the tag to the sample molecule upon cleavage of the cleavable
       functional group.
```

```
L17
     ANSWER 5 OF 21 USPATFULL
       2002:258766 USPATFULL
AN
TI
       Methods for determining a nucleotide at a specific location within a
       nucleic acid molecule
       Smith, Douglas R., Gloucester, MA, UNITED STATES
IN
       Thomann, Hans-Ulrich, Lexington, MA, UNITED STATES
       Cahill, Patrick, Natick, MA, UNITED STATES
       Genome Therapeutics Corporation, Waltham, MA, UNITED STATES, 02154 (U.S.
PΑ
       corporation)
PΙ
       US 2002142336
                               20021003
                          Α1
       US 2002-61961
                               20020201 (10)
AΙ
                          Α1
PRAI
       US 2001-266035P
                           20010202 (60)
DT
       Utility
FS
       APPLICATION
       LAHIVE & COCKFIELD, 28 STATE STREET, BOSTON, MA, 02109
LREP
CLMN
       Number of Claims: 33
ECL
       Exemplary Claim: 1
DRWN
       19 Drawing Page(s)
LN.CNT 2015
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
```

Novel methods for determining the existence or nonexistence of a test nucleotide on a strand of DNA are provided. The methods involve the use of a proofreading polymerase that is capable of incorporating a labeled nucleotide in a primer into and extension product if there is a match between the test nucleotide on the strand of DNA and the complementary nucleotide on the primer, but which excises the labeled nucleotide and does not incorporate it into an extension product if there is a mismatch. The presence or absence of the test nucleotide then may be established by determining whether the label is preserved or lost following the reaction. Methods involving the use of a quencher-chromophore pair are also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

```
ANSWER 6 OF 21 USPATFULL
L17
       2002:251742 USPATFULL
AN
TΤ
       Base analogues
       Kumar, Shiv, Belle Mead, NJ, UNITED STATES
TN
       Nampalli, Satyam, Belle Mead, NJ, UNITED STATES
       Neagu, Constantin, West Windsor, NJ, UNITED STATES
       McDougall, Mark, Arroyo Grande, CA, UNITED STATES
       Loakes, David, Cambridge, UNITED KINGDOM
       Brown, Dan, Cambridge, UNITED KINGDOM
       US 2002137695
PΙ
                          A1
                               20020926
       US 2001-898210
                          Α1
                               20010703 (9)
ΑI
       GB 2000-16258
                           20000703
PRAI
DT
       Utility
       APPLICATION
FS
       Amersham Pharmacia Biotech, Inc., 800 Centennial Avenue, Piscataway, NJ,
LREP
CLMN
       Number of Claims: 17
       Exemplary Claim: 1
ECL
       No Drawings
DRWN
LN.CNT 619
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention describes novel compounds of the formula formula
AB
       ##STR1##
```

Wherein Q is H or a sugar or a sugar analogue or a nucleic acid backbone or backbone analogue, Y=0 O, S, NR.sup.10, where R.sup.10 is H, alkyl alkenyl, alkynyl, X is H, alkyl, alkenyl, alkynyl, aryl, heteroaryl or a combination thereof or, preferably, a reporter group. The novel compounds are suitable for incorporation in **oligonucleotides** and polynucleotides.

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L17
     ANSWER 7 OF 21 USPATFULL
       2002:251113 USPATFULL
AN
TΙ
       Rapid, quantitative method for the mass spectrometric analysis of
       nucleic acids for gene expression and genotyping
       Wold, Barbara J., Pasadena, CA, UNITED STATES
IN
       Murphy, John F., Pasadena, CA, UNITED STATES
       Davis, Mark E., Pasadena, CA, UNITED STATES
       Kirshenbaum, Kent, Pasadena, CA, UNITED STATES Tirrell, David A., Pasadena, CA, UNITED STATES
PΙ
       US 2002137057
                            Α1
                                  20020926
       US 2001-918687
                            A1
                                  20010727 (9)
ΑI
PRAI
       US 2000-221479P
                             20000727 (60)
DT
       Utility
FS
       APPLICATION
LREP
       Lisa A. Haile, J.D., Ph.D., GRAY CARY WARE & FREIDENRICH LLP, 4365
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09567863 Executive Drive, Suite 1600, San Diego, CA, 92121-2189 Number of Claims: 38 CLMN ECL Exemplary Claim: 1 DRWN 25 Drawing Page(s) LN.CNT 1674 CAS INDEXING IS AVAILABLE FOR THIS PATENT. The invention provides methods of identifying one or more nucleic acids AΒ in a sample. The nucleic acids, for example, expressed genes in a cell, can be identified by contacting the nucleic acids with oligonucleotides having detector tags, and selector tags to form tagged oligonucleotides. Each nucleic acid can be uniquely identified by mass-spectrophotometric analysis of the detector tag. CAS INDEXING IS AVAILABLE FOR THIS PATENT. L17 ANSWER 8 OF 21 USPATFULL 2002:198549 USPATFULL ΔM тT Fixed address analysis of sequence tags TN Lizardi, Paul M., Wallingford, CT, UNITED STATES Roth, Matthew E., Branford, CT, UNITED STATES Feng, Li, Hamden, CT, UNITED STATES Guerra, Cesar E., Guilford, CT, UNITED STATES Weber, Shane C., Woodbridge, CT, UNITED STATES Kaufman, Joseph C., Hamden, CT, UNITED STATES Latimer, Darin R., East Haven, CT, UNITED STATES Yale University (U.S. corporation) PA 20020808 US 2002106649 A1PΙ US 2001-855793 20010515 (9) A1 AIContinuation of Ser. No. US 2000-544713, filed on 6 Apr 2000, PATENTED RLIUS 1999-127932P 19990406 (60) PRAI DTUtility APPLICATION FS Robert A. Hodges, NEEDLE & ROSENBERG, P.C., The Candler Building, Suite LREP 1200, 127 Peachtree Street, N.E., Atlanta, GA, 30303-1811 Number of Claims: 154 CLMN Exemplary Claim: 1 ECL5 Drawing Page(s) DRWN LN.CNT 4340 CAS INDEXING IS AVAILABLE FOR THIS PATENT. Disclosed is a method for the comprehensive analysis of nucleic acid samples and a detector composition for use in the method. The method,

referred to as Fixed Address Analysis of Sequence Tags (FAAST), involves generation of a set of nucleic acid fragments having a variety of sticky end sequences; indexing of the fragments into sets based on the sequence of sticky ends; associating a detector sequence with the fragments; sequence-based capture of the indexed fragments on a detector array; and detection of the fragment labels. Generation of the multiple sticky end sequences is accomplished by incubating the nucleic acid sample with one or more nucleic acid cleaving reagents. The indexed fragments are captured by hybridization and coupling, preferably by ligation, to a probe. The method allows a complex sample of nucleic acid to be quickly and easily cataloged in a reproducible and sequence-specific manner. One form of the method allows determination of associations, in a nucleic acid molecule, of different combinations of known or potential sequences. Another form of the method assesses modification of sequences in nucleic acid molecules by basing cleavage of the molecules on the presence or absence of modification.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 9 OF 21 USPATFULL AN 2002:127090 USPATFULL

ΤI

IN

```
PΙ
       US 2002065609
                          A1
                               20020530
ΑI
       US 2001-829855
                          A1
                               20010410 (9)
      US 2000-196063P
                           20000410 (60)
PRAI
                           20000411 (60)
      US 2000-196258P
DT
      Utility
      APPLICATION
FS
       James F. Haley, Jr., FISH & NEAVE, 1251 Avenue of the Americas, New
LREP
       York, NY, 10020-1104
CLMN
      Number of Claims: 44
       Exemplary Claim: 1
ECL
       18 Drawing Page(s)
DRWN
LN.CNT 2019
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention relates to methods for performing surveys of the
       genetic diversity of a population. The invention also relates to methods
       for performing genetic analyses of a population. The invention further
       relates to methods for the creation of databases comprising the survey
       information and the databases created by these methods. The invention
       also relates to methods for analyzing the information to correlate the
       presence of nucleic acid markers with desired parameters in a sample.
       These methods have application in the fields of geochemical exploration,
       agriculture, bioremediation, environmental analysis, clinical
       microbiology, forensic science and medicine.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
    ANSWER 10 OF 21 USPATFULL
L17
       2002:126287 USPATFULL
AN
TI
       Proteomic analysis
       Cravatt, Benjamin F., La Jolla, CA, UNITED STATES
IN
       Sorensen, Erik, San Diego, CA, UNITED STATES
       Patricelli, Matthew P., San Diego, CA, UNITED STATES
       Lovato, Martha, San Diego, CA, UNITED STATES
       Adam, Gregory, San Diego, CA, UNITED STATES
       The Scripps Research Institute of an Assignment (U.S. corporation)
PA
PΙ
       US 2002064799
                          Α1
                               20020530
AΙ
       US 2001-836145
                          Α1
                               20010416 (9)
       Continuation of Ser. No. US 2000-738271, filed on 15 Dec 2000, PENDING
RLI
PRAI
       US 2000-195954P
                           20000410 (60)
       US 2000-212891P
                           20000620 (60)
                           20000802 (60)
       US 2000-222532P
DT
       Utility
FS
       APPLICATION
       Lisa A. Haile, Ph.D., Gray Cary Ware & Freidenrich LLP, Suite 1600, 4365
LREP
       Executive Drive, San Diego, CA, 92121-2189
       Number of Claims: 13
CLMN
ECL
       Exemplary Claim: 1
       24 Drawing Page(s)
LN.CNT 3602
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention provides methods for analyzing proteomes, as cells
       or lysates. The analysis is based on the use of probes that have
       specificity to the active form of proteins, particularly enzymes and
       receptors. The probes can be identified in different ways. In accordance
       with the present invention, a method is provided for generating and
       screening compound libraries that are used for the identification of
       lead molecules, and for the parallel identification of their biological
       targets. By appending specific functionalities and/or groups to one or
       more binding moieties, the reactive functionalities gain binding
       affinity and specificity for particular proteins and classes of
```

Methods for the survey and genetic analysis of populations

Ashby, Matthew, Mill Valley, CA, UNITED STATES

proteins. Such libraries of candidate compounds, referred to herein as activity-based probes, or ABPs, are used to screen for one or more desired biological activities or target proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

```
L17 ANSWER 11 OF 21 USPATFULL
       2002:85154 USPATFULL
AN
TI
       Proteomic analysis
       Cravatt, Benjamin F., La Jolla, CA, UNITED STATES
TN
       Sorensen, Erik, San Diego, CA, UNITED STATES
       Patricelli, Matthew P., San Diego, CA, UNITED STATES
       Lovato, Martha, San Diego, CA, UNITED STATES
       Adam, Gregory, San Diego, CA, UNITED STATES
                               20020418
       US 2002045194
                          A1
PT
       US 2000-738954
                               20001215 (9)
                          A1
AΤ
      US 2000-195954P
                          20000410 (60)
PRAT
       US 2000-212891P
                           20000620 (60)
       US 2000-222532P
                           20000802 (60)
       Utility
DT
       APPLICATION
FS
       Lisa A. Haile, Ph.D., Gray Cary Ware & Freidenrich LLP, Suite 1600, 4365
LREP
       Executive Drive, San Diego, CA, 92121-2189
       Number of Claims: 31
CLMN
       Exemplary Claim: 1
ECL
DRWN
       24 Drawing Page(s)
LN.CNT 3728
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention provides methods for analyzing proteomes, as cells
AB
       or lysates. The analysis is based on the use of probes that have
       specificity to the active form of proteins, particularly enzymes and
       receptors. The probes can be identified in different ways. In accordance
       with the present invention, a method is provided for generating and
       screening compound libraries that are used for the identification of
       lead molecules, and for the parallel identification of their biological
       targets. By appending specific functionalities and/or groups to one or
       more binding moieties, the reactive functionalities gain binding
       affinity and specificity for particular proteins and classes of
       proteins. Such libraries of candidate compounds, referred to herein as
       activity-based probes, or ABPs, are used to screen for one or more
       desired biological activities or target proteins.
```

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ANSWER 12 OF 21 USPATFULL
L17
       2002:73134 USPATFULL
AN
ΤI
       Proteomic analysis
       Cravatt, Benjamin F., La Jolla, CA, UNITED STATES
IN
       Sorensen, Erik, San Diego, CA, UNITED STATES
       Patricelli, Matthew P., San Diego, CA, UNITED STATES
       Lovato, Martha, San Diego, CA, UNITED STATES
       Adam, Gregory, San Diego, CA, UNITED STATES
       The Scripps Research Institute (U.S. corporation)
PΑ
PI
       US 2002040275
                          A1
                               20020404
                               20010416 (9)
ΑI
       US 2001-836148
                          A1
       Continuation of Ser. No. US 2000-738954, filed on 15 Dec 2000, PENDING
RLI
                           20000410 (60)
PRAI
       US 2000-195954P
                           20000620 (60)
       US 2000-212891P
       US 2000-222532P
                           20000802 (60)
       Utility
DT
FS
       APPLICATION
       Lisa A. Haile, Ph.D., Gray Cary Ware & Freidenrich LLP, Suite 1600, 4365
LREP
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Executive Drive, San Diego, CA, 92121-2189

CLMN Number of Claims: 15 ECL Exemplary Claim: 1 DRWN 24 Drawing Page(s)

LN.CNT 3667

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention provides methods for analyzing proteomes, as cells or lysates. The analysis is based on the use of probes that have specificity to the active form of proteins, particularly enzymes and receptors. The probes can be identified in different ways. In accordance with the present invention, a method is provided for generating and screening compound libraries that are used for the identification of lead molecules, and for the parallel identification of their biological targets. By appending specific functionalities and/or groups to one or more binding moieties, the reactive functionalities gain binding affinity and specificity for particular proteins and classes of proteins. Such libraries of candidate compounds, referred to herein as activity-based probes, or ABPs, are used to screen for one or more desired biological activities or target proteins.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 13 OF 21 USPATFULL

AN 2002:43173 USPATFULL

TI Methods for preparing conjugates

IN Dellinger, Douglas J., Sunnyvale, CA, UNITED STATES Myerson, Joel, Berkeley, CA, UNITED STATES Fulcrand, Geraldine, Sunnyvale, CA, UNITED STATES Ilsley, Diane D., San Jose, CA, UNITED STATES

PI US 2002025539 A1 20020228

AI US 2001-981580 A1 20011017 (9)

RLI Division of Ser. No. US 1999-397526, filed on 16 Sep 1999, PENDING

DT Utility

FS APPLICATION

LREP AGILENT TECHNOLOGIES, INC., Legal Department, DL429, Intellectual Property Administration, P. O. Box 7599, Loveland, CO, 80537-0599

CLMN Number of Claims: 45 ECL Exemplary Claim: 1 DRWN 2 Drawing Page(s)

LN.CNT 1750

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Methods are disclosed for conjugating one moiety to another moiety. In the method the moieties are reacted with one another in a protic solvent. Reaction between the moieties and the protic solvent during the conjugating is negligible or reversible. A stable bond is formed between the moieties to produce a product that is not subject to .beta.-elimination at elevated pH. Usually, one of the moieties comprises an unsaturation between two carbon atoms. One of the carbon atoms is or becomes an electrophile during the conjugating. The other of the moieties comprises a functionality reactive with the electrophile carbon atom to form a product that comprises the unsaturation. Compounds comprising both of the moieties as well as precursor molecules are also disclosed. Methods are also disclosed for determining an analyte in a sample employing compounds as described above.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 14 OF 21 USPATFULL

AN 2002:298463 USPATFULL

TI Parallel methods for genomic analysis

IN Strathmann, Michael P., 1674 Euclid Ave., Berkeley, CA, United States 94709

L17 ANSWER 16 OF 21 USPATFULL

Base analoques

2002:224621 USPATFULL

AN

ΤI

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PΙ
       US 6480791
                        B1
                               20021112
       US 1999-427834
                               19991026 (9)
ΑI
       US 1998-105914P
PRAI
                         19981028 (60)
DT
       Utility
       GRANTED
EXNAM Primary Examiner: Brusca, John S.; Assistant Examiner: Moran, Marjorie
       McCutchen, Doyle, Brown & Enersen, LLP, Shuster, Michael J.
LREP
       Number of Claims: 30
CLMN
       Exemplary Claim: 1
ECL
       10 Drawing Figure(s); 8 Drawing Page(s)
DRWN
LN.CNT 4843
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention provides parallel methods for determining
       nucleotide sequences and physical maps of polynucleotides associated
       with sample tags. This information can be used to determine the
       chromosomal locations of sample-tagged polynucleotides. In one
       embodiment, the polynucleotides are derived from genomic DNA coupled to
       insertion elements. As a result, the invention also provides parallel
       methods for locating the integration sites of insertion elements in the
       genome.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L17 ANSWER 15 OF 21 USPATFULL
       2002:262204 USPATFULL
AN
       Methods for controlling cross-hybridization in analysis of nucleic acid
TT
       sequences
       Wolber, Paul K., Los Altos, CA, United States
TN
       Kincaid, Robert H., Half Moon Bay, CA, United States
       Agilent Technologies, Inc., Palo Alto, CA, United States (U.S.
PΑ
       corporation)
                               20021008
PΙ
       US 6461816
                         B1
       US 1999-350969
                               19990709 (9)
ΑI
DT
       Utility
       GRANTED
FS
EXNAM Primary Examiner: Brusca, John S.; Assistant Examiner: Kim, Young
       Number of Claims: 28
CLMN
       Exemplary Claim: 1
ECL
DRWN
       0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 2702
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Methods, reagents and kits are disclosed for selecting target-specific
ΔR
       oligonucleotide probes, which may be used in analyzing a target
       nucleic acid sequence. In one aspect the present invention is directed
       to selecting a set of target-specific oligonucleotide probes.
       A cross-hybridization oligonucleotide probe is identified
       based on a candidate target-specific oligonucleotide probe for
       the target nucleic acid sequence. The cross-hybridization
       oligonucleotide probe measures the extent of occurrence of a
       cross-hybridization event having a predetermined probability.
       Cross-hybridization results are determined employing the
       cross-hybridization oligonucleotide probe and the
       target-specific oligonucleotide probe. The target-specific
       oligonucleotide probe is selected or rejected for the set based
       on the cross-hybridization results.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
```

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Simmonds, Adrian Christopher, Amersham, UNITED KINGDOM
TN
       Hamilton, Alan, Amersham, UNITED KINGDOM
       Smith, Clifford, Tring, UNITED KINGDOM
       Loakes, David, Letchworth, UNITED KINGDOM
       Brown, Daniel, Cambridge, UNITED KINGDOM
       Hill, Fergal, Cambridge, UNITED KINGDOM
       Kumar, Shiv, Belle Mead, NJ, United States
       Nampalli, Satyam, Belle Mead, NJ, United States
       McDougall, Mark, Bethlehem, PA, United States
       Nycomed Amersham PLC, Buckinghamshire, UNITED KINGDOM (non-U.S.
PA
       corporation)
       US 6444682
                                20020903
PΙ
                           B1
       US 2000-463501
                                20000418 (9)
ΑI
PRAI
       GB 1997-16231
                            19970731
DT
       Utility
       GRANTED
FS
       Primary Examiner: Shah, Mukund J.; Assistant Examiner: Patel, Sudhaker
EXNAM
       Marshall, Gerstein & Borun
LREP
       Number of Claims: 14
CLMN
ECL
       Exemplary Claim: 1
       0 Drawing Figure(s); 0 Drawing Page(s)
DRWN
LN.CNT 1300
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Nucleotide or base analogues having structure (3) or (4) ##STR1##
AΒ
       wherein X.dbd.O or NH or S and
       each R.sup.6 is independently H or alkyl or alkenyl or alkoxy or aryl or
       a reporter moiety.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 17 OF 21 USPATFULL
L17
AN
       2002:136767 USPATFULL
       Analysis of sequence tags with hairpin primers
ΤI
IN
       Lizardi, Paul M., Wallingford, CT, United States
       Latimer, Darin R., East Haven, CT, United States
Yale University, New Haven, CT, United States (U.S. corporation)
PA
PΙ
       US 6403319
                           B1
                                20020611
       US 2000-637384
                                20000811 (9)
AΤ
       Continuation-in-part of Ser. No. US 2000-544713, filed on 6 Apr 2000,
RLI
       now patented, Pat. No. US 6261782
PRAI
       US 1999-148870P
                            19990813 (60)
DT
       Utility
FS
       GRANTED
EXNAM
       Primary Examiner: Horlick, Kenneth R.
       Needle & Rosenberg, P.C.
LREP
CLMN
       Number of Claims: 106
ECL
       Exemplary Claim: 1
DRWN
       7 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 3134
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Disclosed is a method for the comprehensive analysis of nucleic acid
       samples and a detector composition for use in the method. The method
       involves amplifying nucleic acid fragments of interest using a primer
       that can form a hairpin structure; sequence-based coupling of the
       amplified fragments to detector probes; and detection of the coupled
       fragments. The amplified fragments are coupled by hybridization and
       coupling, preferably by ligation, to detector probes. A hairpin
       structure formed at the end of the amplified fragments facilitates
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coupling of the fragments to the probes. The method allows detection of

the fragments where detection provides some sequence information for the fragments. The method allows a complex sample of nucleic acid to be quickly and easily cataloged in a reproducible and sequence-specific manner. The method can also be used to detect amplified fragments having a known sequence.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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ANSWER 18 OF 21 USPATFULL
L17
       2002:102268 USPATFULL
AN
ΤI
       Binary encoded sequence tags
       Kaufman, Joseph C., Hamden, CT, United States
IN
       Roth, Matthew E., Branford, CT, United States
       Lizardi, Paul M., Wallingford, CT, United States
       Feng, Li, Hamden, CT, United States
       Latimer, Darin R., East Haven, CT, United States
       Yale University, United States (U.S. corporation)
PA
       Agilix Corporation, United States (U.S. corporation)
PТ
       US 6383754
                          В1
                               20020507
      US 2000-637751
                               20000811 (9)
ΑI
       Continuation-in-part of Ser. No. US 2000-544713, filed on 6 Apr 2000,
RLI
       now patented, Pat. No. US 6261782
       US 1999-148870P
                           19990813 (60)
PRAI
DT
      Utility
FS
       GRANTED
      Primary Examiner: Horlick, Kenneth R.
EXNAM
      Needle & Rosenberg, P.C.
LREP
      Number of Claims: 131
CLMN
ECL
      Exemplary Claim: 1
DRWN
       3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 3871
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Disclosed is a method for the comprehensive analysis of nucleic acid
ΔR
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samples and a detector composition for use in the method. The method, referred to as Binary Encoded Sequence Tags (BEST), involves generation of a set of nucleic acid fragments; adding an adaptor to the ends containing recognition site for cleavage at a site offset from the recognition site; cleaving the fragment to generate fragments having a plurality sticky ends; indexing of the fragments into sets based on the sequence of sticky ends. The fragments are indexed by adding a offset adaptor to newly generated ends. A different adaptor will be coupled to each different sticky end. The resulting fragments -- which will have defined ends, be of equal lengths (in preferred embodiment), and a central sequence derived from the source nucleic acid molecule -- are binary sequence tags. The binary sequence tags can be used and further analyzed in numerous ways. For example, the binary sequence tags can be captured by hybridization and coupling, preferably by ligation, to a probe. The probe is preferably immobilized in an array or on sortable beads. One form of the BEST method, referred to as modification assisted analysis of binary sequence tags (MAABST), assesses modification of sequences in nucleic acid molecules by detecting differential cleavage based on the presence or absence of modification in the molecules.

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L17 ANSWER 19 OF 21 USPATFULL

AN 2001:112050 USPATFULL

TI Fixed address analysis of sequence tags

IN Lizardi, Paul M., Wallingford, CT, United States
Roth, Matthew E., Branford, CT, United States
Feng, Li, Hamden, CT, United States
Guerra, Cesar E., Guilford, CT, United States
```

```
Yale University, New Haven, CT, United States (U.S. corporation)
PΑ
PI
       US 6261782
                         B1
                               20010717
       US 2000-544713
                               20000406 (9)
ΑI
PRAI
       US 1999-127932P
                         19990406 (60)
       Utility
DT
       GRANTED
EXNAM Primary Examiner: Horlick, Kenneth R.
       Needle & Rosenberg, P.C.
LREP
CLMN
       Number of Claims: 154
       Exemplary Claim: 1
ECL
       5 Drawing Figure(s); 5 Drawing Page(s)
DRWN
LN.CNT 4505
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Disclosed is a method for the comprehensive analysis of nucleic acid
       samples and a detector composition for use in the method. The method,
       referred to as Fixed Address Analysis of Sequence Tags (FAAST), involves
       generation of a set of nucleic acid fragments having a variety of sticky
       end sequences; indexing of the fragments into sets based on the sequence
       of sticky ends; associating a detector sequence with the fragments;
       sequence-based capture of the indexed fragments on a detector array; and
       detection of the fragment labels. Generation of the multiple
       sticky end sequences is accomplished by incubating the nucleic acid
       sample with one or more nucleic acid cleaving reagents. The indexed
       fragments are captured by hybridization and coupling, preferably by
       ligation, to a probe. The method allows a complex sample of nucleic acid
       to be quickly and easily cataloged in a reproducible and
       sequence-specific manner. One form of the method allows determination of
       associations, in a nucleic acid molecule, of different combinations of
       known or potential sequences. Another form of the method assesses
       modification of sequences in nucleic acid molecules by basing cleavage
       of the molecules on the presence or absence of modification.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L17 ANSWER 20 OF 21 USPATFULL
       2001:56106 USPATFULL
AN
ΤI
       Compounds and methods for detecting biomolecules
       Rothschild, Kenneth J., Newton, MA, United States
IN
       Olejnik, Jerzy, Brookline, MA, United States
       AmberGen Inc., Boston, MA, United States (U.S. corporation)
PA
       US 6218530
PΙ
                         В1
                               20010417
      US 1999-323424
ΑI
                               19990601 (9)
      US 1998-87641P
PRAI
                          19980602 (60)
DT
      Utility
FS
       Granted
EXNAM Primary Examiner: Riley, Jezia
      Medlen & Carroll, LLP
LREP
      Number of Claims: 12
CLMN
ECL
       Exemplary Claim: 1
       10 Drawing Figure(s); 9 Drawing Page(s)
LN.CNT 728
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Methods are described for synthesizing compounds useful for detecting
       nucleic acids, and in particular, the hybridization of nucleic acids.
       Photocleavable agents are described, including but not limited to
       photocleavable nucleotides and photocleavable phosphoramidites.
```

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Weber, Shane C., Woodbridge, CT, United States Kaufman, Joseph C., Hamden, CT, United States Latimer, Darin R., East Haven, CT, United States

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L17
    ANSWER 21 OF 21 USPATFULL
       2001:55695 USPATFULL
AN
       Method and mixture reagents for analyzing the nucleotide sequence of
ΤI
       nucleic acids by mass spectrometry
       Sampson, Jeffrey R., Burlingame, CA, United States
IN
       Yakhini, Zohar H., Palo Alto, CA, United States
       Webb, Peter G., Menlo Park, CA, United States
       Sampas, Nicholas M., San Jose, CA, United States
       Tsalenko, Anna M., Chicago, IL, United States
       Myerson, Joel, Berkeley, CA, United States
       Agilent Technologies, Inc., Palo Alto, CA, United States (U.S.
PA
       corporation)
PΙ
       US 6218118
                          В1
                               20010417
       US 1998-112437
                               19980709 (9)
ΑI
DT
      Utility
      Granted
FS
     Primary Examiner: Horlick, Kenneth R.; Assistant Examiner: Siew, Jeffrey
EXNAM
      Number of Claims: 70
CLMN
ECL
       Exemplary Claim: 1
       26 Drawing Figure(s); 22 Drawing Page(s)
DRWN
LN.CNT 2982
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      Methods and reagents are disclosed which satisfy the need for more
AB
       sensitive, more accurate and higher through-put analyses of target
       nucleic acid sequences. The methods and reagents may be generically
       applied to generally any target nucleic acid sequence and do not require
       a priori information about the presence, location or identity of
      mutations in the target nucleic acid sequence. The reagents of the
       invention are mixtures of natural and mass-modified
       oligonucleotide precursors having a high level of coverage and
      mass number complexity. A method is also disclosed for analyzing a
       target nucleic acid sequence employing the mixtures of natural and
      mass-modified oligonucleotide precursors and chemical or
       enzymatic assays to alter the mass of the oligonucleotide
      precursors prior to mass spectral analysis, generally via MALDI-TOF. The
       enzymatic assay may be a polymerase extension assay or a ligase assay.
       The kits for carrying out the methods of the invention are also
       disclosed.
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=>
=> d his
     (FILE 'HOME' ENTERED AT 10:12:59 ON 18 DEC 2002)
     FILE 'BIOSIS, MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 10:13:34 ON
     18 DEC 2002
         343861 S NUCLEIC ACID
L1
              2 S L1 AND POSITIV? (3A) CHARGE TAG (3A) NUCLEIC ACID?
L_2
             21 S L1 AND POSITIV? (4A) CHARG? (3A) TAG?
L3
L4
             19 S L3 NOT L2
             19 DUP REM L4 (0 DUPLICATES REMOVED)
L5
            109 S L1 AND POSITIV? (4A) LABEL
L6
            108 S L6 NOT L5
L7
             92 S L7 AND PHOSPHAT?
L8
             92 DUP REM L8 (0 DUPLICATES REMOVED)
Ь9
L10
             22 S L9 AND POSITIV? (4A) CHARG?
              1 S POSITIV? (3A) CHARG? (3A) LABEL? (4A) TERMINAL (4A) (NUCLEIC
L11
              1 S L11 AND POSITIV?
L12
            110 S MASS TAG
L13
             50 S L13 AND OLIGONUCLEOTIDE?
L14
             43 S L14 AND LABEL?
L15
             21 S L15 AND TERMINAL
L16
             21 DUP REM L16 (0 DUPLICATES REMOVED)
L17
=> s positiv? charg? label? oligonucleotide?
             1 POSITIV? CHARG? LABEL? OLIGONUCLEOTIDE?
L18
=> d 118 bib abs
    ANSWER 1 OF 1 USPATFULL
       2002:236261 USPATFULL
AN
ΤI
       Charge tags and the separation of nucleic acid molecules
IN
       Lyamichev, Victor, Madison, WI, UNITED STATES
       Skrzpczynski, Zbigniew, Verona, WI, UNITED STATES
       Allawi, Hatim T., Madison, WI, UNITED STATES
       Wayland, Sarah R., Madison, WI, UNITED STATES
       Takova, Tsetska, Madison, WI, UNITED STATES
       Neri, Bruce P., Madison, WI, UNITED STATES
       Third Wave Technologies, Inc. (U.S. corporation)
PA
PI
       US 2002128465
                          A1
                               20020912
                               20010206 (9)
ΑI
       US 2001-777430
                          A1
       Continuation-in-part of Ser. No. US 1999-333145, filed on 14 Jun 1999,
RLI
       PENDING Continuation-in-part of Ser. No. US 1996-682853, filed on 12 Jul
       1996, GRANTED, Pat. No. US 6001567
DT
       Utility
FS
       APPLICATION
       MEDLEN & CARROLL, LLP, 101 HOWARD STREET, SUITE 350, SAN FRANCISCO, CA,
LREP
       94105
CLMN
       Number of Claims: 86
ECL
       Exemplary Claim: 1
DRWN
       46 Drawing Page(s)
LN.CNT 5163
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB
       The present invention relates to novel phosphoramidites, including
       positive and neutrally charged compounds. The present invention also
       provides charge tags for attachment to materials including solid
       supports and nucleic acids, wherein the charge tags increase or decrease
       the net charge of the material. The present invention further provides
       methods for separating and characterizing molecules based on the charge
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09567863

differentials between modified and unmodified materials. CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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=> d 123 1-2 bib abs ANSWER 1 OF 2 WPIDS (C) 2002 THOMSON DERWENT L23 2002-674850 [72] WPIDS AN CR 1997-393613 [36] DNC C2002-190055 Composition useful for e.g. separation of nucleic acids comprises a TΙ positively or neutrally charged phosphoramidite. DC B04 B05 D16 ALLAWI, H T; LYAMICHEV, V; NERI, B P; SKRZPCZYNSKI, Z; TAKOVA, T; WAYLAND, IN (THIR-N) THIRD WAVE TECHNOLOGIES INC PΑ CYC 100 WO 2002063030 A2 20020815 (200272)* EN 197p PΙ RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW US 2002128465 A1 20020912 (200272) ADT WO 2002063030 A2 WO 2002-US3423 20020206; US 2002128465 A1 CIP of US 1996-682853 19960712, CIP of US 1999-333145 19990614, US 2001-777430 20010206 FDT US 2002128465 A1 CIP of US 6001567 PRAI US 2001-777430 20010206; US 1996-682853 19960712; US 1999-333145 19990614 2002-674850 [72] WPIDS AN CR 1997-393613 [36] WO 200263030 A UPAB: 20021108 AΒ NOVELTY - Composition comprises a positively or neutrally charged phosphoramidite. DETAILED DESCRIPTION - Composition (c) or (c') comprises a positively charged phosphoramidite of formula (I) or a neutrally charged phosphoramidite of formula (II). (I) comprises nitrogen-containing chemical group selected from primary, secondary or tertiary amine or ammonium group. (II) comprises secondary or tertiary amine or ammonium group. X, Z = a reactive phosphate group; Y = a protected hydroxy group; X' = a protected hydroxy group; N, N' = an amine group. INDEPENDENT CLAIMS are included for the following: (1) a composition (c1) comprising a charge tag (x1) attached to a terminal end of a nucleic acid molecule, the charge tag comprises a phosphate group and a positively charged molecule; (2) a composition (c2) comprising a nucleic acid molecule that comprises a positively charged phosphoramidite; (3) a composition (c3) comprising a charge tag attached to the terminal end of a nucleic acid molecule, the charge tag comprises a positively charged phosphoramidite; (4) a composition (c4) comprising a fluorescent dye directly bonded to a phosphate group, which is not directly bonded to an amine

(5) a mixture (m) comprising a number of oligonucleotides, each oligonucleotide is attached to a different charge tag with each charge tag comprising a phosphate group and a positively charged group;

(6) a composition (c5) comprising a solid support attached to a charged tag, the charge tag comprises a positively charged group and a reactive group configured to allow the charge tag to covalently attach to

the nucleic acid molecule;

- (7) separating nucleic acid molecules involving either:
- (a) treating (m1) a charge-balanced oligonucleotide containing the charge tag to produce a charge-unbalanced oligonucleotide and separating the charge-unbalanced oligonucleotide from the reaction mixture; or
- (b) treating (m2) a number of charge-balanced oligonucleotides, each containing different charge tags, to produce at least 2 charge-unbalanced oligonucleotides, and separating the charge-unbalanced oligonucleotides from the reaction mixture.

USE - The composition is useful for separation of nucleic acid molecules (claimed). The composition is further useful for fractionation of specific nucleic acids by selective charge reversal useful in e.g. INVADER assay cleavage reactions; and in the synthesis of charge-balanced molecules.

ADVANTAGE - In the fractionation of nucleic acid molecules, the method provides an absolute readout of the partition of products from substrates (i.e. provides a 100% separation). Through the use of multiple positively charged adducts, synthetic molecules can be constructed with sufficient modification due to the fact that the normally negatively charged strand is made nearly neutral. It is also possible to distinguish between a enzymatically or thermally degraded DNA fragments due to the absence or presence of 3'phosphate.

Dwg.0/46

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L23 ANSWER 2 OF 2 USPATFULL
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AN 2002:236261 USPATFULL

TI Charge tags and the separation of nucleic acid molecules

IN Lyamichev, Victor, Madison, WI, UNITED STATES
Skrzpczynski, Zbigniew, Verona, WI, UNITED STATES
Allawi, Hatim T., Madison, WI, UNITED STATES
Wayland, Sarah R., Madison, WI, UNITED STATES
Takova, Tsetska, Madison, WI, UNITED STATES
Neri, Bruce P., Madison, WI, UNITED STATES

PA Third Wave Technologies, Inc. (U.S. corporation)

PI US 2002128465 A1 20020912

AI US 2001-777430 A1 20010206 (9)

RLI Continuation-in-part of Ser. No. US 1999-333145, filed on 14 Jun 1999, PENDING Continuation-in-part of Ser. No. US 1996-682853, filed on 12 Jul 1996, GRANTED, Pat. No. US 6001567

DT Utility

FS APPLICATION

LREP MEDLEN & CARROLL, LLP, 101 HOWARD STREET, SUITE 350, SAN FRANCISCO, CA, 94105

CLMN Number of Claims: 86 ECL Exemplary Claim: 1

DRWN 46 Drawing Page(s)

LN.CNT 5163

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention relates to novel phosphoramidites, including positive and neutrally charged compounds. The present invention also provides charge tags for attachment to materials including solid supports and nucleic acids, wherein the charge tags increase or decrease the net charge of the material. The present invention further provides methods for separating and characterizing molecules based on the charge differentials between modified and unmodified materials.

DRWN

LN.CNT 15696

16 Drawing Page(s)

=> d 124 bib abs 1-21 ANSWER 1 OF 21 USPATFULL AΝ 2002:290760 USPATFULL TΙ PARG, a GTPase activating protein which interacts with PTPL1 Saras, Jan, Uppsala, SWEDEN IN Franzen, Petra, Uppsala, SWEDEN Aspenstrom, Pontus, Uppsala, SWEDEN Hellman, Ulf, Uppsala, SWEDEN Gonez, Leonel Jorge, Victoria, AUSTRALIA Heldin, Carl-Henrik, Uppsala, SWEDEN PA Ludwig Institute for Cancer Research, New York, NY, United States (U.S. corporation) US 6475775 PΙ В1 20021105 US 2000-566076 20000508 (9) АΤ Division of Ser. No. US 1998-80855, filed on 18 May 1998, now patented, RLI Pat. No. US 6083721 Continuation of Ser. No. US 1997-805583, filed on 25 Feb 1997, now abandoned DT Utility GRANTED FS EXNAM Primary Examiner: McKelvey, Terry Wolf, Greenfield & Sacks, P.C. LREP Number of Claims: 11 CLMN Exemplary Claim: 1 ECL DRWN 12 Drawing Figure(s); 10 Drawing Page(s) LN.CNT -2870 CAS INDEXING IS AVAILABLE FOR THIS PATENT. The invention describes nucleic acids encoding the PARG protein, AB including fragments and biologically functional variants thereof. Also included are polypeptides and fragments thereof encoded by such nucleic acids, and antibodies relating thereto. Methods and products for using such nucleic acids and polypeptides also are provided. CAS INDEXING IS AVAILABLE FOR THIS PATENT. L24 ANSWER 2 OF 21 USPATFULL AN 2002:272761 USPATFULL ΤI Directed evolution of novel binding proteins Ladner, Robert Charles, Ijamsville, MD, UNITED STATES IN Guterman, Sonia Kosow, Belmont, MA, UNITED STATES Roberts, Bruce Lindsay, Milford, MA, UNITED STATES Markland, William, Milford, MA, UNITED STATES Ley, Arthur Charles, Newton, MA, UNITED STATES Kent, Rachel Baribault, Boxborough, MA, UNITED STATES PΙ US 2002150881 20021017 Α1 US 2001-781988 20010214 (9) ΑI A1 RLI Continuation of Ser. No. US 1998-192067, filed on 16 Nov 1998, ABANDONED Continuation of Ser. No. US 1995-415922, filed on 3 Apr 1995, PATENTED Continuation of Ser. No. US 1993-9319, filed on 26 Jan 1993, PATENTED Division of Ser. No. US 1991-664989, filed on 1 Mar 1991, PATENTED Continuation-in-part of Ser. No. US 1990-487063, filed on 2 Mar 1990, ABANDONED Continuation-in-part of Ser. No. US 1988-240160, filed on 2 Sep 1988, ABANDONED PRAI WO 1989-US3731 19890901 Utility DTFS APPLICATION LREP BROWDY AND NEIMARK, P.L.L.C., 624 Ninth Street, N.W., Washington, DC, 20001 CLMN Number of Claims: 18 ECL Exemplary Claim: 1

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin inhibitor, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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ANSWER 3 OF 21 USPATFULL
L24
       2002:243051 USPATFULL
AN
       Compositions and methods for the therapy and diagnosis of ovarian cancer
TΤ
       Algate, Paul A., Issaquah, WA, UNITED STATES
IN
       Jones, Robert, Seattle, WA, UNITED STATES
       Harlocker, Susan L., Seattle, WA, UNITED STATES
       Corixa Corporation, Seattle, WA, UNITED STATES, 98104 (U.S. corporation)
PA
      US 2002132237
PΙ
                         A1
                               20020919
      US 2001-867701
                               20010529 (9)
ΑI
                          A1
      US 2000-207484P
PRAI
                           20000526 (60)
DT
      Utility
FS
      APPLICATION
      SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVE, SUITE 6300,
LREP
      SEATTLE, WA, 98104-7092
      Number of Claims: 11
CLMN
ECL
      Exemplary Claim: 1
DRWN
      No Drawings
LN.CNT 25718
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Compositions and methods for the therapy and diagnosis of cancer,
AB
      particularly ovarian cancer, are disclosed. Illustrative compositions
       comprise one or more ovarian tumor polypeptides, immunogenic portions
       thereof, polynucleotides that encode such polypeptides, antigen
```

presenting cell that expresses such polypeptides, and T cells that are

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L24 ANSWER 4 OF 21 USPATFULL
AN
       2002:242791 USPATFULL
       Compositions and methods for the therapy and diagnosis of colon cancer
ΤI
      King, Gordon E., Shoreline, WA, UNITED STATES
IN
      Meagher, Madeleine Joy, Seattle, WA, UNITED STATES
      Xu, Jiangchun, Bellevue, WA, UNITED STATES
      Secrist, Heather, Seattle, WA, UNITED STATES
PA
      Corixa Corporation, Seattle, WA, UNITED STATES (U.S. corporation)
PΙ
      US 2002131971
                         A1
                               20020919
      US 2001-33528
AΙ
                         A1
                               20011226 (10)
RLI
      Continuation-in-part of Ser. No. US 2001-920300, filed on 31 Jul 2001,
```

specific for cells expressing such polypeptides. The disclosed compositions are useful, for example, in the diagnosis, prevention

and/or treatment of diseases, particularly ovarian cancer.

PENDING

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PRAI
       US 2001-302051P
                           20010629 (60)
       US 2001-279763P
                           20010328 (60)
       US 2000-223283P
                           20000803 (60)
DT
       Utility
       APPLICATION
FS
LREP
       SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVE, SUITE 6300,
       SEATTLE, WA, 98104-7092
       Number of Claims: 17
CLMN
       Exemplary Claim: 1
ECL
       No Drawings
DRWN
LN.CNT 8083
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Compositions and methods for the therapy and diagnosis of cancer,
       particularly colon cancer, are disclosed. Illustrative compositions
       comprise one or more colon tumor polypeptides, immunogenic portions
       thereof, polynucleotides that encode such polypeptides, antigen
       presenting cell that expresses such polypeptides, and T cells that are
       specific for cells expressing such polypeptides. The disclosed
       compositions are useful, for example, in the diagnosis, prevention
       and/or treatment of diseases, particularly colon cancer.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
    ANSWER 5 OF 21 USPATFULL
L24
       2002:51095 USPATFULL
AN
ΤI
       Peptides comprising repetitive units of amino acids and DNA sequences
       encoding the same
       Ferrari, Franco A., La Jolla, CA, United States
TN
       Richardson, Charles, Florence, MT, United States
       Chambers, James, San Diego, CA, United States
       Causey, Stuart, Palo Alto, CA, United States
       Pollock, Thomas J., San Diego, CA, United States
       Cappello, Joseph, San Diego, CA, United States
       Crissman, John W., San Diego, CA, United States
       Protein Polymer Technologies, Inc., San Diego, CA, United States (U.S.
PA
       corporation)
       US 6355776
PI
                          В1
                               20020312
       US 1999-444791
ΑI
                               19991122 (9)
       Continuation of Ser. No. US 1995-482085, filed on 7 Jun 1995, now
RLI
       patented, Pat. No. US 6018030 Continuation-in-part of Ser. No. US
       1993-175155, filed on 29 Dec 1993, now patented, Pat. No. US 5641648,
       issued on 24 Jun 1997 Continuation-in-part of Ser. No. US 1993-53049,
       filed on 22 Apr 1993, now abandoned Continuation of Ser. No. US
       1987-114618, filed on 29 Oct 1987, now patented, Pat. No. US 5243038,
       issued on 7 Sep 1993 Continuation-in-part of Ser. No. US 1986-927258,
       filed on 4 Nov 1986, now abandoned
DT
       Utility
FS
       GRANTED
EXNAM
      Primary Examiner: McKelvey, Terry; Assistant Examiner: Sandals, William
       Flehr Hohbach Test Albritton & Herbert LLP, Trecartin, Esq., Richard F.
LREP
CLMN
       Number of Claims: 5
ECL
       Exemplary Claim: 1
       14 Drawing Figure(s); 10 Drawing Page(s)
DRWN
LN.CNT 5152
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AΒ
       Novel polypeptides comprising repetitive units of amino acids, as well
       as synthetic genes encoding the subject polypeptides are provided. The
       subject polypeptides are characterized by comprising repetitive units of
       amino acids, where the repetitive units are present in naturally
       occurring proteins, particularly naturally occurring structural
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proteins. The subject polypeptides find use in a variety of

applications, such as structural components of prosthetic devices, synthetic fibers, and the like.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

```
ANSWER 6 OF 21 USPATFULL
L24
AN
       2001:226757 USPATFULL
       Transferrin receptor reactive chimeric antibodies
TΤ
       Friden, Phillip M., Bedford, MA, United States
IN
       Alkermes, Inc., Cambridge, MA, United States (U.S. corporation)
PΑ
                               20011211
PΙ
       US 6329508
                          В1
       WO 9310819 19930610
                               19940705 (8)
ΑI
       US 1994-232246
       WO 1992-US10206
                               19921124
                               19940705 PCT 371 date
                               19940705 PCT 102(e) date
       Continuation-in-part of Ser. No. US 1991-800458, filed on 26 Nov 1991,
RLI
       now abandoned Continuation-in-part of Ser. No. WO 1990-US5077, filed on
       7 Sep 1990 Continuation-in-part of Ser. No. US 1989-404089, filed on 7
       Sep 1989, now patented, Pat. No. US 5154924
DT
       Utility
       GRANTED
FS
      Primary Examiner: Huff, Sheela
EXNAM
       Hamilton Brook Smith & Reynolds, P.C.
LREP
       Number of Claims: 4
CLMN
ECL
       Exemplary Claim: 1
       79 Drawing Figure(s); 77 Drawing Page(s)
DRWN
LN.CNT 1687
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention pertains to chimeric antibodies that are reactive
       with transferrin receptors on brain capillary endothelial cells. These
       antibodies are composed of a variable region, immunologically reactive
       with the transferrin receptors, that is obtained from one animal source,
       and a constant region that is derived from an animal source other than
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the one that provided the variable region. These chimeric antibodies can

neuropharmaceutical agent for transferal across the blood brain barrier.

exist either as isolated entities or as conjugates with a

```
ANSWER 7 OF 21 USPATFULL
L24
       2001:196825 USPATFULL
AN
TI
       Complementary DNAs
IN
       Edwards, Jean-Baptiste Dumas Milne, Paris, France
       Duclert, Aymeric, Saint Maur, France
       Bougueleret, Lydie, Vanves, France
PA
       Genset, Paris, France (non-U.S. corporation)
PΙ
       US 6312922
                                20011106
                                19990209 (9)
AΙ
       US 1999-247155
PRAI
       US 1998-74121P
                            19980209 (60)
       US 1998-81563P
                            19980413 (60)
       US 1998-96116P
                            19980810 (60)
       US 1998-99273P
                            19980904 (60)
       US 1998-96116P
                            19980904 (60)
       US 1998-99273P
                            19980904 (60)
       US 1998-99273P
                            19980904 (60)
       US 1998-96116P
                            19980904 (60)
       US 1998-99273P
                            19980904 (60)
       US 1998-99273P
                            19980904 (60)
       US 1998-99273P
                           19980904 (60)
DT
       Utility
FS
       GRANTED
```

DΤ

Utility

```
EXNAM Primary Examiner: Brusca, John S.
       Knoibbe, Martens, Olson & Bear, LLP
       Number of Claims: 33
CLMN
ECL
       Exemplary Claim: 32
       12 Drawing Figure(s); 10 Drawing Page(s)
DRWN
LN.CNT 6339
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The sequences of extended cDNAs encoding secreted proteins are
       disclosed. The extended cDNAs can be used to express secreted proteins
       or portions thereof or to obtain antibodies capable of specifically
       binding to the secreted proteins. The extended cDNAs may also be used in
       diagnostic, forensic, gene therapy, and chromosome mapping procedures.
       The extended cDNAs may also be used to design expression vectors and
       secretion vectors.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L24
    ANSWER 8 OF 21 USPATFULL
       2001:60048 USPATFULL
ΑN
       5' ESTs for secreted proteins expressed in brain
TТ
       Edwards, Jean-Baptiste Dumas Milne, Paris, France
IN
       Duclert, Aymeric, Saint Maur, France
       Lacroix, Bruno, Saint-Genis Laval, France
       Genset, Paris, France (non-U.S. corporation)
PA
PΤ
       US 6222029
                               20010424
                         B1
       US 1997-905223
                               19970801 (8)
ΑI
       Utility
DT
FS
       Granted
EXNAM Primary Examiner: Priebe, Scott D.
       Knobbe Martens Olson & Bear LLP
LREP
CLMN
       Number of Claims: 20
ECL
       Exemplary Claim: 1,3,5,7,9
DRWN
       7 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 4221
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The sequences of 5' ESTs derived from mRNAs encoding secreted proteins
AB
       are disclosed. The 5' ESTs may be to obtain cDNAs and genomic DNAs
       corresponding to the 5' ESTs. The 5' ESTs may also be used in
       diagnostic, forensic, gene therapy, and chromosome mapping procedures.
       Upstream regulatory sequences may also be otained using the 5' ESTs. The
       5' ESTs may also be used to design expression vectors and secretion
       vectors.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
    ANSWER 9 OF 21 USPATFULL
AN
       2000:84062 USPATFULL
TI
       Isolated nucleic acid molecules encoding PARG, a GTPase activating
       protein which interacts with PTPL1
IN
       Saras, Jan, Uppsala, Sweden
       Franzen, Petra, Uppsala, Sweden
       Aspenstrom, Pontus, Uppsala, Sweden
       Hellman, Ulf, Uppsala, Sweden
       Gonez, Leonel Jorge, Hughesdale, Australia
       Heldin, Carl-Henrik, Uppsala, Sweden
PΑ
       Ludwig Institute for Cancer Research, New York, NY, United States (U.S.
       corporation)
PΙ
       US 6083721
                               20000704
ΑI
       US 1998-80855
                               19980518 (9)
RLI
       Continuation-in-part of Ser. No. US 1997-805583, filed on 25 Feb 1997,
       now abandoned
```

09567863 FS Granted EXNAM Primary Examiner: McKelvey, Terry LREP Wolf, Greenfield & Sacks, P.C. Number of Claims: 24 CLMN ECL Exemplary Claim: 1 DRWN 12 Drawing Figure(s); 10 Drawing Page(s) LN.CNT 3145 CAS INDEXING IS AVAILABLE FOR THIS PATENT. The invention describes nucleic acids encoding the PARG protein, including fragments and biologically functional variants thereof. Also included are polypeptides and fragments thereof encoded by such nucleic acids, and antibodies relating thereto. Methods and products for using such nucleic acids and polypeptides also are provided. CAS INDEXING IS AVAILABLE FOR THIS PATENT. ANSWER 10 OF 21 USPATFULL L24 AN 2000:10019 USPATFULL TIencoding the same

Peptides comprising repetitive units of amino acids and DNA sequences

Ferrari, Franco A., La Jolla, CA, United States IN Richardson, Charles, Florence, MT, United States Chambers, James, San Diego, CA, United States Causey, Stuart, Palo Alto, CA, United States Pollock, Thomas J., San Diego, CA, United States Cappello, Joseph, San Diego, CA, United States Crissman, John W., San Diego, CA, United States

Protein Polymer Technologies, Inc., San Diego, CA, United States (U.S. PΑ corporation)

PΤ US 6018030 20000125 19950607 (8) US 1995-482085 ΑI

Continuation-in-part of Ser. No. US 1993-175155, filed on 29 Dec 1993, RLI now patented, Pat. No. US 5641648 which is a continuation-in-part of Ser. No. US 1993-53049, filed on 22 Apr 1993, now abandoned which is a continuation of Ser. No. US 1987-114618, filed on 29 Oct 1987, now patented, Pat. No. US 5243038, issued on 7 Sep 1993 which is a continuation-in-part of Ser. No. US 1986-927258, filed on 4 Nov 1986, now abandoned

DTUtility FS Granted

EXNAM Primary Examiner: Degen, Nancy; Assistant Examiner: Sandals, William

Trecartin, Richard F.Flehr Hohbach Test Albritton & Herbert LLP LREP

Number of Claims: 19 CLMN Exemplary Claim: 1 ECL

DRWN 14 Drawing Figure(s); 10 Drawing Page(s)

LN.CNT 6111

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Polypeptides comprising repetitive units of amino acids, as well as synthetic genes encoding the subject polypeptides are provided. The subject polypeptides are characterized by comprising repetitive units of amino acids, where the repetitive units are present in naturally occurring proteins, particularly naturally occurring structural proteins. The subject polypeptides find use in a variety of applications, such as structural components of prosthetic devices, synthetic fibers, and the like.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L24ANSWER 11 OF 21 USPATFULL

AN 2000:7057 USPATFULL

TΙ Transferrin receptor specific antibody-neuropharmaceutical or diagnostic agent conjugates

```
Friden, Phillip M., Bedford, MA, United States
IN
       Alkermes, Inc., Cambridge, MA, United States (U.S. corporation)
PA
                               20000118
PΙ
       US 6015555
ΑI
       US 1995-444644
                               19950519 (8)
       Division of Ser. No. US 232246
RLI
DT
       Utility
FS
       Granted
EXNAM Primary Examiner: Burke, Julie
      Hamilton, Brook, Smith & Reynolds, P.C.
LREP
CLMN
      Number of Claims: 6
ECL
       Exemplary Claim: 1
DRWN
       79 Drawing Figure(s); 77 Drawing Page(s)
LN.CNT 3966
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention pertains to a method for delivering a
ΔR
       neuropharmaceutical or diagnostic agent across the blood brain barrier
       to the brain of a host. The method comprises administering to the host a
       therapeutically effective amount of an antibody-neuropharmaceutical or
       diagnostic agent conjugate wherein the antibody is reactive with a
       transferrin receptor and the antibody is a chimera between the variable
       region from one animal source and the constant region from a different
       animal source. Other aspects of this invention include a delivery system
       comprising an antibody reactive with a transferrin receptor linked to a
       neuropharmaceutical or diagnostic agent and methods for treating hosts
       afflicted with a disease associated with a neurological disorder.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
    ANSWER 12 OF 21 USPATFULL
L24
       1998:143904 USPATFULL
AN
TI
       Directed evolution of novel binding proteins
       Ladner, Robert Charles, Ijamsville, MD, United States
TN
       Gutterman, Sonia Kosow, Belmont, MA, United States
       Roberts, Bruce Lindsay, Milford, MA, United States
       Markland, William, Milford, MA, United States
       Ley, Arthur Charles, Newton, MA, United States
       Kent, Rachel Baribault, Boxborough, MA, United States
       Dyax, Corp., Cambridge, MA, United States (U.S. corporation)
PA
       US 5837500
ΡI
                               19981117
       US 1995-415922
                               19950403 (8)
AΙ
       Continuation of Ser. No. US 1993-9319, filed on 26 Jan 1993, now
RLI
       patented, Pat. No. US 5403484 which is a division of Ser. No. US
       1991-664989, filed on 1 Mar 1991, now patented, Pat. No. US 5223409
       which is a continuation-in-part of Ser. No. US 1990-487063, filed on 2
       Mar 1990, now abandoned which is a continuation-in-part of Ser. No. US
       1988-240160, filed on 2 Sep 1988, now abandoned
DT
      Utility
FS
       Granted
EXNAM Primary Examiner: Ulm, John
      Cooper, Iver P.
LREP
CLMN
      Number of Claims: 43
ECL
       Exemplary Claim: 1
       16 Drawing Figure(s); 16 Drawing Page(s)
LN.CNT 15973
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       In order to obtain a novel binding protein against a chosen target, DNA
       molecules, each encoding a protein comprising one of a family of similar
       potential binding domains and a structural signal calling for the
       display of the protein on the outer surface of a chosen bacterial cell,
      bacterial spore or phage (genetic package) are introduced into a genetic
      package. The protein is expressed and the potential binding domain is
       displayed on the outer surface of the package. The cells or viruses
```

bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin inhibitor, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

```
ANSWER 13 OF 21 USPATFULL
L24
       1998:134864 USPATFULL
ΑN
      Methods for preparing synthetic repetitive DNA
ΤI
IN
      Ferrari, Franco A., La Jolla, CA, United States
       Cappello, Joseph, San Diego, CA, United States
       Crissman, John W., San Diego, CA, United States
      Dorman, Mary A., San Diego, CA, United States
       Protein Polymer Technologies, Inc., San Diego, CA, United States (U.S.
PA
      corporation)
      US 5830713
                               19981103
PΙ
      US 1996-707237
                               19960903 (8)
AΙ
      Continuation-in-part of Ser. No. US 1993-175155, filed on 29 Dec 1993,
RLI
      now patented, Pat. No. US 5641648 which is a continuation-in-part of
      Ser. No. US 1993-53049, filed on 22 Apr 1993, now abandoned which is a
      continuation-in-part of Ser. No. US 1990-609716, filed on 6 Nov 1990,
      now patented, Pat. No. US 5514581, issued on 7 May 1996 which is a
      continuation-in-part of Ser. No. US 1988-269429, filed on 9 Nov 1988,
      now abandoned which is a continuation-in-part of Ser. No. US
       1987-114618, filed on 19 Oct 1987, now patented, Pat. No. US 5243038,
       issued on 7 Sep 1993 which is a continuation-in-part of Ser. No. US
       1986-927258, filed on 4 Nov 1986, now abandoned
DT
      Utility
FS
      Granted
EXNAM
      Primary Examiner: Degen, Nancy
      Trecartin, Richard F., Kresnak, Mark T. Flehr Hohbach Test Albritton and
LREP
      Herbert
CLMN
      Number of Claims: 37
ECL
      Exemplary Claim: 1
       14 Drawing Figure(s); 10 Drawing Page(s)
LN.CNT 5084
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      Methods are provided for the production of large polypeptides containing
      repeating sequences of amino acids utilizing biochemical techniques,
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specifically DNA sequences coding for the expression of the large polypeptides. Systems utilizing exogenous transcriptional and translational regions to control the production of the large

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

polypeptides are also provided.

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L24 ANSWER 14 OF 21 USPATFULL

AN 1998:88695 USPATFULL

TI DNA encoding recombinant lipoprotein antigens

IN Smith, Richard S., Del Mar, CA, United States
Curtiss, Linda K., San Diego, CA, United States
Koduri, Kanaka Raju, San Diego, CA, United States
Witztum, Joseph L., San Diego, CA, United States
Young, Stephen G., Hillsborough, CA, United States

PA The Scripps Research Institute, LaJolla, CA, United States (U.S.
```

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corporation)
                               19980728
PΙ
       US 5786206
       US 1994-333577
                               19941031 (8)
ΑI
       Division of Ser. No. US 1992-959946, filed on 8 Oct 1992, now patented,
RLI
       Pat. No. US 5408038 which is a continuation-in-part of Ser. No. US
       1992-901706, filed on 18 Jun 1992, now abandoned which is a continuation
       of Ser. No. US 1991-774633, filed on 9 Oct 1991, now abandoned
DT
       Utility
       Granted
FS
       Primary Examiner: Wax, Robert A.; Assistant Examiner: Lau, Kawai
EXNAM
       Welsh & Katz, Ltd.
LREP
CLMN
       Number of Claims: 12
       Exemplary Claim: 10
ECL
       7 Drawing Figure(s); 7 Drawing Page(s)
DRWN
LN.CNT 3015
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Methods and compositions are described for determining the level of low
       density lipoproteins (LDL) in plasma. Native apoprotein B-100 (apo
       B-100) present in LDL particles is immunologically mimicked by a
       polypeptide of the invention. A polypeptide includes an amino acid
       residue sequence corresponding to a pan epitope region of the target
       apoprotein. A preferred polypeptide is a fusion protein that
       simultaneously mimics native apo B-100 and native apo A-I. Improved
       assay systems and methods for determining HDL and LDL levels in a body
       fluid sample are also described.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L24
     ANSWER 15 OF 21 USPATFULL
AN
       1998:72720 USPATFULL
       Peptides comprising repetitive units of amino acids and DNA sequences
TΤ
       encoding the same
       Ferrari, Franco A., La Jolla, CA, United States
TN
       Richardson, Charles, Florence, MT, United States
       Chambers, James, San Diego, CA, United States
       Causey, Stuart, Palo Alto, CA, United States
       Pollock, Thomas J., San Diego, CA, United States
       Cappello, Joseph, San Diego, CA, United States
       Crissman, John W., San Diego, CA, United States
       Protein Polymer Technologies, Inc., San Diego, CA, United States (U.S.
PΑ
       corporation)
       US 5770697
PI
                               19980623
       US 1995-477509
                               19950607 (8)
ΑI
       Continuation-in-part of Ser. No. US 1993-175155, filed on 29 Dec 1993,
RLT
       now patented, Pat. No. US 5641648, issued on 24 Jun 1997 which is a
       continuation-in-part of Ser. No. US 1993-53049, filed on 22 Apr 1993,
       now abandoned which is a continuation of Ser. No. US 1987-114618, filed
       on 29 Oct 1987, now patented, Pat. No. US 5243038, issued on 7 Sep 1993
       which is a continuation-in-part of Ser. No. US 1986-927258, filed on 4
       Nov 1986, now abandoned
DT
       Utility
FS
       Granted
EXNAM
       Primary Examiner: Ketter, James; Assistant Examiner: Brusca, John S.
LREP
       Trecartin, Richard F.
CLMN
       Number of Claims: 16
ECL
       Exemplary Claim: 1
DRWN
       14 Drawing Figure(s); 10 Drawing Page(s)
LN.CNT 3242
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Novel polypeptides comprising repetitive units of amino acids, as well
       as synthetic genes encoding the subject polypeptides are provided. The
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subject polypeptides are characterized by comprising repetitive units of

amino acids, where the repetitive units are present in naturally occurring proteins, particularly naturally occurring structural proteins. The subject polypeptides find use in a variety of applications, such as structural components of prosthetic devices, synthetic fibers, and the like.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 16 OF 21 USPATFULL 97:54100 USPATFULL AN Methods for preparing synthetic repetitive DNA ΤI IN Ferrari, Franco A., La Jolla, CA, United States Cappello, Joseph, San Diego, CA, United States Richardson, Charles, Florence, MT, United States Protein Polymer Technologies, Inc., San Diego, CA, United States (U.S. PA corporation) US 5641648 19970624 PΙ ΑI US 1993-175155 19931229 (8) Continuation-in-part of Ser. No. US 1993-53049, filed on 22 Apr 1993, RLI now abandoned which is a continuation of Ser. No. US 1987-114618, filed on 29 Oct 1987, now patented, Pat. No. US 5243038 And a continuation-in-part of Ser. No. US 1990-609716, filed on 6 Nov 1990, now patented, Pat. No. US 5514581 which is a continuation-in-part of Ser. No. US 1988-269429, filed on 9 Nov 1988, now abandoned which is a continuation-in-part of Ser. No. US 1987-114618, filed on 29 Oct 1987, now patented, Pat. No. US 5243038 which is a continuation-in-part of Ser. No. US 1986-927258, filed on 4 Nov 1986, now abandoned DTUtility FS Granted EXNAM Primary Examiner: Fleisher, Mindy; Assistant Examiner: Degen, Nancy J. Flehr Hohbach Test Albritton & Herbert LLP LREP CLMN Number of Claims: 20 ECL Exemplary Claim: 1 14 Drawing Figure(s); 10 Drawing Page(s) DRWN LN.CNT 3033 CAS INDEXING IS AVAILABLE FOR THIS PATENT. Methods are provided for the production of large polypeptides containing AB repeating sequences of amino acids utilizing biochemical techniques, specifically DNA sequences coding for the expression of the large polypeptides. Systems utilizing exogenous transcriptional and translational regions to control the production of the large polypeptides are also provided.

```
L24 ANSWER 17 OF 21 USPATFULL
       96:101466 USPATFULL
AN
ΤI
       Directed evolution of novel binding proteins
IN
       Ladner, Robert C., Ijamsville, MD, United States
       Guterman, Sonia K., Belmont, MA, United States
       Roberts, Bruce L., Milford, MA, United States Markland, William, Milford, MA, United States
       Ley, Arthur C., Newton, MA, United States
       Kent, Rachel B., Boxborough, MA, United States
PΑ
       Protein Engineering Corporation, Cambridge, MA, United States (U.S.
       corporation)
PΙ
       US 5571698
                                 19961105
ΑI
       US 1993-57667
                                 19930618 (8)
DCD
       20100629
RLI
       Continuation of Ser. No. US 1991-664989, filed on 1 Mar 1991, now
       patented, Pat. No. US 5223409 which is a continuation-in-part of Ser.
       No. US 1990-487063, filed on 2 Mar 1990, now abandoned which is a
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continuation-in-part of Ser. No. US 1988-240160, filed on 2 Sep 1988, now abandoned Utility DТ FS Granted Primary Examiner: Ulm, John EXNAM Cooper, Iver P. CLMN Number of Claims: 83 Exemplary Claim: 1 ECL 16 Drawing Figure(s); 16 Drawing Page(s) DRWN LN.CNT 15323 CAS INDEXING IS AVAILABLE FOR THIS PATENT. In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin inhibitor, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein. CAS INDEXING IS AVAILABLE FOR THIS PATENT. L24 ANSWER 18 OF 21 USPATFULL AN 95:34283 USPATFULL TINonnatural apolipoprotein B-100 peptides and apolipoprotein B-100-apolipoprotein A-I fusion peptides Smith, Richard S., Del Mar, CA, United States IN Curtiss, Linda K., San Diego, CA, United States Koduri, Kanaka R., San Diego, CA, United States Witztum, Joseph L., San Diego, CA, United States Young, Stephen G., Hillsborough, CA, United States PA The Scripps Research Institute, La Jolla, CA, United States (U.S. corporation) ΡI US 5408038 19950418 US 1992-959946 ΑI 19921008 (7) Continuation-in-part of Ser. No. US 1992-901706, filed on 18 Jun 1992, RLI now abandoned which is a continuation of Ser. No. US 1991-774633, filed on 9 Oct 1991, now abandoned DT Utility Granted Primary Examiner: Parr, Margaret; Assistant Examiner: Schreiber, David EXNAM Welsh & Katz LREP Number of Claims: 12 CLMN Exemplary Claim: 1 ECL 7 Drawing Figure(s); 7 Drawing Page(s) LN.CNT 2961 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Methods and compositions are described for determining the level of low density lipoproteins (LDL) in plasma. Native apoprotein B-100 (apo B-100) present in LDL particles is immunologically mimicked by a polypeptide of the invention. A polypeptide includes an amino acid residue sequence corresponding to a pan epitope region of the target apoprotein. A preferred polypeptide is a fusion protein that

simultaneously mimics native apo B-100 and native apo A-I. Improved assay systems and methods for determining HDL and LDL levels in a body fluid sample are also described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

```
L24
    ANSWER 19 OF 21 USPATFULL
       95:29292 USPATFULL
AN
       Viruses expressing chimeric binding proteins
TI
       Ladner, Robert C., Ijamsville, MD, United States
IN
       Guterman, Sonia K., Belmont, MA, United States
       Roberts, Bruce L., Milford, MA, United States
       Markland, William, Milford, MA, United States
       Ley, Arthur C., Newton, MA, United States
       Kent, Rachel B., Boxborough, MA, United States
       Protein Engineering Corporation, Cambridge, MA, United States (U.S.
PΑ
       corporation)
PΙ
       US 5403484
                               19950404
ΔΤ
       US 1993-9319
                               19930126 (8)
      Division of Ser. No. US 1991-664989, filed on 1 Mar 1991, now patented,
RLT
       Pat. No. US 5223409 which is a continuation-in-part of Ser. No. US
       1990-487063, filed on 2 Mar 1990, now abandoned which is a
       continuation-in-part of Ser. No. US 1988-240160, filed on 2 Sep 1988,
       now abandoned
      WO 1989-3731
                           19890901
PRAI
      Utility
DТ
FS
      Granted
EXNAM Primary Examiner: Hill, Jr., Robert J.; Assistant Examiner: Ulm, John D.
      Cooper, Iver P.
LREP
      Number of Claims: 49
CLMN
ECL
       Exemplary Claim: 1
       16 Drawing Figure(s); 16 Drawing Page(s)
DRWN
LN.CNT 14368
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       In order to obtain a novel binding protein against a chosen target, DNA
AB
```

molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin inhibitor, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

```
L24 ANSWER 20 OF 21 USPATFULL

AN 93:52487 USPATFULL

TI Directed evolution of novel binding proteins

IN Ladner, Robert C., Ijamsville, MD, United States
Guterman, Sonia K., Belmont, MA, United States
Roberts, Bruce L., Milford, MA, United States
Markland, William, Milford, MA, United States
Ley, Arthur C., Newton, MA, United States
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Kent, Rachel B., Boxborough, MA, United States
       Protein Engineering Corp., Cambridge, MA, United States (U.S.
PΑ
       corporation)
PΙ
       US 5223409
                               19930629
       US 1991-664989
                               19910301 (7)
ΔΤ
       Continuation-in-part of Ser. No. US 1990-487063, filed on 2 Mar 1990,
RLI
       now abandoned And a continuation-in-part of Ser. No. US 1988-240160,
       filed on 2 Sep 1988, now abandoned
DT
       Utility
       Granted
FS
EXNAM Primary Examiner: Hill, Jr., Robert J.; Assistant Examiner: Ulm, John D.
       Cooper, Iver P.
LREP
       Number of Claims: 66
CLMN
ECL
       Exemplary Claim: 1
       16 Drawing Figure(s); 16 Drawing Page(s)
DRWN
LN.CNT 15410
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       In order to obtain a novel binding protein against a chosen target, DNA
AB
       molecules, each encoding a protein comprising one of a family of similar
       potential binding domains and a structural signal calling for the
       display of the protein on the outer surface of a chosen bacterial cell,
       bacterial spore or phage (genetic package) are introduced into a genetic
       package. The protein is expressed and the potential binding domain is
       displayed on the outer surface of the package. The cells or viruses
       bearing the binding domains which recognize the target molecule are
       isolated and amplified. The successful binding domains are then
       characterized. One or more of these successful binding domains is used
       as a model for the design of a new family of potential binding domains,
       and the process is repeated until a novel binding domain having a
       desired affinity for the target molecule is obtained. In one embodiment,
       the first family of potential binding domains is related to bovine
       pancreatic trypsin inhibitor, the genetic package is M13 phage, and the
       protein includes the outer surface transport signal of the M13 gene III
       protein.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L24
    ANSWER 21 OF 21 USPATFULL
       90:48734 USPATFULL
AN
ΤI
       Expression of higher eucaryotic genes in aspergillus
       McKnight, Gary L., Seattle, WA, United States
TN
       Upshall, Alan, Bothell, WA, United States
PA
       ZymoGenetics, Inc., Seattle, WA, United States (U.S. corporation)
                               19900619
ΡI
       US 4935349
       US 1987-946873
                               19870109 (6)
AΙ
       Continuation-in-part of Ser. No. US 1986-820519, filed on 17 Jan 1986,
RLI
       now abandoned
       Utility
DT
FS
       Granted
      Primary Examiner: Weimar, Elizabeth C.; Assistant Examiner: Peet,
EXNAM
       Richard C.
LREP
       Seed and Berry
CLMN
       Number of Claims: 10
ECL
       Exemplary Claim: 8
       33 Drawing Figure(s); 28 Drawing Page(s)
DRWN
LN.CNT 1406
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       A method for expressing higher eucaryotic genes in Aspergillus through
       the use of a recombinant plasmid capable of integration into the
       chromosomal DNA of Aspergillus is disclosed. It is preferred to utilize
       a transcriptional promoter within a DNA construct contained in the
       plasmid that is of a DNA sequence encoding an ADH enzyme or a TPI
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09567863

enzyme. Promoters capable of directing the expression of a heterologous gene in Aspergillus, as well as other filamentous fungal genera are also disclosed.

d his

(FILE 'HOME' ENTERED AT 10:12:59 ON 18 DEC 2002)

21 S L22 NOT L23

FILE 'BIOSIS, MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 10:13:34 ON 18 DEC 2002 L1 343861 S NUCLEIC ACID 2 S L1 AND POSITIV? (3A) CHARGE TAG (3A) NUCLEIC ACID? L_2 21 S L1 AND POSITIV? (4A) CHARG? (3A) TAG? L3 19 S L3 NOT L2 L419 DUP REM L4 (0 DUPLICATES REMOVED) L5 L6 109 S L1 AND POSITIV? (4A) LABEL L7 108 S L6 NOT L5 92 S L7 AND PHOSPHAT? L8 92 DUP REM L8 (0 DUPLICATES REMOVED) L9 22 S L9 AND POSITIV? (4A) CHARG? L10 1 S POSITIV? (3A) CHARG? (3A) LABEL? (4A) TERMINAL (4A) (NUCLEIC L11L121 S L11 AND POSITIV? L13110 S MASS TAG 50 S L13 AND OLIGONUCLEOTIDE? L1443 S L14 AND LABEL? L15 21 S L15 AND TERMINAL L1621 DUP REM L16 (0 DUPLICATES REMOVED) L171 S POSITIV? CHARG? LABEL? OLIGONUCLEOTIDE? L181 S POSITIV? (4A) CHARG? LABEL? (3A) OLIGONUCLEOTIDE? L19 117 S POSITIV? (5A) (LABEL? OR TAG?) (4A) OLIGONUCLEOTIDE? L2031 S L20 AND AMINE L2123 S L21 AND AMMONIUM L222 S L22 AND PHOSPHORAMIDITE L23

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L24

=> d 128 bib abs 1-16 L28 ANSWER 1 OF 16 WPIDS (C) 2002 THOMSON DERWENT ΔN 2002-075320 [10] WPIDS DNC C2002-022504 Detecting nucleic acid e.g. for detecting single TInucleotide polymorphisms by fluorescence hybridization involves use of nucleic acid probes comprising neutral or positively charged fluorescent label. DC B04 D16 JEONG, S; NIKIFOROV, T T IN (CALI-N) CALIPER TECHNOLOGIES CORP; (JEON-I) JEONG S; (NIKI-I) NIKIFOROV T PΑ CYC 23 WO 2001088195 A1 20011122 (200210)* EN PΙ 69p RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR W: AU CA JP AU 2001061523 A 20011126 (200222) US 2002037520 A1 20020328 (200225) WO 2001088195 A1 WO 2001-US15427 20010511; AU 2001061523 A AU 2001-61523 ADT 20010511; US 2002037520 A1 Provisional US 2000-203723P 20000512, US 2001-854417 20010511 AU 2001061523 A Based on WO 200188195 FDT PRAI US 2000-203723P 20000512; US 2001-854417 20010511 2002-075320 [10] WPIDS WO 200188195 A UPAB: 20020213 AB NOVELTY - Detecting (M1) nucleic acid, comprising contacting first nucleic acid to second nucleic acid which comprises neutral or positively charged fluorescent label, and detecting fluorescence polarization (FP) of the resulting mixture of first and second nucleic acids, is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a system (I) comprising: (a) a container having a duplexed nucleic acid, where at least one strand of the nucleic acid duplex has a neutral or positively charged fluorescent label; (b) a polarized light source positioned to shine plant polarized light through a portion of the container, thereby exciting the fluorescent label during operation of the system; and (c) a detector that detects resultant polarization of light emitted by the fluorescent label; (2) a microfluidic fluorescent polarization nucleic acid analysis system, comprising: (a) a microfluidic device comprising a body structure having at least two microfluidic channels disposed in it; (b) a source of a first nucleic acid; (c) a source of a second nucleic acid comprises a neutral or positively charged fluorescent label; (d) a source of plane polarized light, which source is positioned to illuminate a portion of at lest one of the least two microchannels; and (e) a fluorescence polarization detector positioned to detect plane polarized light emitted form the microfluidic device; and (3) a computer implemented process in an assay system for quantifying nucleic acid hybridization parameter, where the assay system involves: (a) providing first nucleic acid composition comprising first nucleic acid having positive or neutral fluorescent label; (b) introducing second nucleic acid into first

nucleic acid composition to provide a second

nucleic acid composition, the second nucleic
acid reacting with the first nucleic acid to
produce a fluorescently labeled product having a substantially different
rotation rate than the first nucleic acid;

- (c) determining a first level of fluorescence polarization of the first nucleic acid composition;
- (d) determining a second level of fluorescence polarization of the second nucleic acid composition;
- (e) comparing the first and second levels of fluorescent polarization; and
- (f) calculating the nucleic acid hybridization parameter.

USE - Detecting a nucleic acid by contacting first nucleic acid such as DNA, RNA, LNA (locked nucleic acid), DNA or RNA analog, or peptide nucleic acid (PNA). (M1) is useful for identifying the presence of a subsequence of nucleotides in a target nucleic acid, comprising contacting target nucleic acid with a labeled nucleic acid probe that comprises a neutral or positively charged label comprising a fluorophore to form a first reaction mixture, and detecting the level of FP of first reaction mixture. The target nucleic acid sequences comprises at least one locus for single nucleotide polymorphism (SNP) and the nucleic acid probe is complementary to one allele of SNP in the target nucleic acid sequence. Optionally, the method preferably involves contacting several additional target nucleic acids with several additional nucleic acid probes, each of which comprises a neutral or positively charged label comprising a fluorophore to form several additional reaction mixture, and detecting the level of FP of several additional reaction mixture. Each of the additional target nucleic acid comprises a locus for SNP and each of the several additional probes are complementary to at least one allele of each of the SNPs in the target nucleic acid sequences derived from a single species, variety, cultivar, cell, virus, or organism. The identification of SNPs provides a SNP genotype for the species, variety, cultivar, cell, virus or organism. (All claimed). (M1) is useful for detecting single nucleotide polymorphisms and in a method of genotyping a nucleic acid sample. The microfluidic devices are useful for performing high throughput screening assays in drug discovery, immunoassays, diagnostics, and genetic analysis.

ADVANTAGE - The method is simple, and is less biased. The use of neutral or positively charged fluorescent labels on nucleic acid probes results in a relatively large change in observed FP of the probe labeled during nucleic acid hybridization. Preferably, addition of polylysine (a positively charged linker) to first and second nucleic acids increases FP by less than 50 %. Dwg.0/12

filed on 26 Nov 1996, ABANDONED Continuation-in-part of Ser. No. US

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L28 ANSWER 2 OF 16 USPATFULL
       2002:329806 USPATFULL
AN
TI
       Invasion assays
IN
       Hall, Jeff G., Madison, WI, UNITED STATES
       Lyamichev, Victor I., Madison, WI, UNITED STATES
       Mast, Andrea L., Madison, WI, UNITED STATES
       Brow, Mary Ann D., Madison, WI, UNITED STATES
PI
       US 2002187486
                          A1
                               20021212
AΙ
       US 2001-33297
                          A1
                               20011102 (10)
RLI
       Continuation of Ser. No. US 1999-350597, filed on 9 Jul 1999, PENDING
       Continuation of Ser. No. US 1997-823516, filed on 24 Mar 1997, GRANTED,
       Pat. No. US 5994069 Continuation-in-part of Ser. No. US 1996-756038,
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1996-756386, filed on 26 Nov 1996, GRANTED, Pat. No. US 5985557 Continuation-in-part of Ser. No. US 1996-682853, filed on 12 Jul 1996, GRANTED, Pat. No. US 6001567 Continuation-in-part of Ser. No. US 1996-599491, filed on 24 Jan 1996, GRANTED, Pat. No. US 5846717 DTUtility APPLICATION FS MEDLEN & CARROLL, LLP, Suite 350, 101 Howard Street, San Francisco, CA, LREP 94105 Number of Claims: 34 CLMN ECL Exemplary Claim: 1 121 Drawing Page(s) DRWN LN.CNT 10560 The present invention relates to means for the detection and AB characterization of nucleic acid sequences, as well as variations in nucleic acid sequences. The present invention also relates to methods for forming a nucleic acid cleavage structure on a target sequence and cleaving the nucleic acid cleavage structure in a site-specific manner. The structure-specific nuclease activity of a variety of enzymes is used to cleave the target-dependent cleavage structure, thereby indicating the presence of specific nucleic acid sequences or specific variations thereof. The present invention further relates to methods and devices for the separation of nucleic acid molecules based on charge. The present invention also provides methods for the detection of non-target cleavage products via the formation of a complete and activated protein binding region. The invention further provides sensitive and specific methods for the detection of human cytomegalovirus nucleic acid in a sample. L28 ANSWER 3 OF 16 USPATFULL 2002:254176 USPATFULL AN Detection of nucleic acids by multiple sequential invasive cleavages 02 TI Hall, Jeff G., Madison, WI, United States IN Lyamichev, Victor I., Madison, WI, United States Mast, Andrea L., Madison, WI, United States Brow, Mary Ann D., Madison, WI, United States Third Wave Technologies, Inc. Madison, WI, United States (U.S. PA corporation) PΙ US 6458535 20021001 В1 US 1999-350597 19990709 (9) AΙ Continuation of Ser. No. US 1997-823516, filed on 24 Mar 1997, now RLI patented, Pat. No. US 5994069 Continuation-in-part of Ser. No. US 1996-759038, filed on 2 Dec 1996, now patented, Pat. No. US 6090543 Continuation-in-part of Ser. No. US 1996-756386, filed on 26 Nov 1996, now patented, Pat. No. US 5085557 Continuation-in-part of Ser. No. US 1996-682853, filed on 12 Jul 1996, now patented, Pat. No. US 6001567 Continuation-in-part of Ser. No. US 1996-599491, filed on 24 Jan 1996, now patented, Pat. No. US 5846717, issued on 8 Dec 1998 DT Utility FS GRANTED EXNAM Primary Examiner: Jones, W. Gary; Assistant Examiner: Souaya, Jehanne LREP Medlen & Carroll, LLP Number of Claims: 27 CLMN ECL Exemplary Claim: 1 170 Drawing Figure(s); 128 Drawing Page(s) DRWN LN.CNT 13831 CAS INDEXING IS AVAILABLE FOR THIS PATENT. The present invention relates to means for the detection and

characterization of nucleic acid sequences, as well as variations in nucleic acid sequences. The present

invention also relates to methods for forming a nucleic acid cleavage structure on a target sequence and cleaving the nucleic acid cleavage structure in a site-specific manner. The structure-specific nuclease activity of a variety of enzymes is used to cleave the target-dependent cleavage structure, thereby indicating the presence of specific nucleic acid sequences or specific variations thereof. The present invention further relates to methods and devices for the separation of nucleic acid molecules based on charge. The present invention also provides methods for the detection of non-target cleavage products via the formation of a complete and activated protein binding region. The invention further provides sensitive and specific methods for the detection of human cytomegalovirus nucleic acid in a sample.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L28 ANSWER 4 OF 16 USPATFULL
       2002:236261 USPATFULL
AN
TI
       Charge tags and the separation of nucleic acid
      molecules
      Lyamichev, Victor, Madison, WI, UNITED STATES
TN
       Skrzpczynski, Zbigniew, Verona, WI, UNITED STATES
      Allawi, Hatim T., Madison, WI, UNITED STATES
       Wayland, Sarah R., Madison, WI, UNITED STATES
       Takova, Tsetska, Madison, WI, UNITED STATES
      Neri, Bruce P., Madison, WI, UNITED STATES
      Third Wave Technologies, Inc. (U.S. corporation)
PA
PΙ
      US 2002128465
                               20020912
                          A1
AΙ
      US 2001-777430
                          A1
                               20010206 (9)
      Continuation-in-part of Ser. No. US 1999-333145, filed on 14 Jun 1999,
RLI
      PENDING Continuation-in-part of Ser. No. US 1996-682853, filed on 12 Jul
      1996, GRANTED, Pat. No. US 6001567
DT
      Utility
FS
      APPLICATION
LREP
      MEDLEN & CARROLL, LLP, 101 HOWARD STREET, SUITE 350, SAN FRANCISCO, CA,
      94105
CLMN
      Number of Claims: 86
ECL
      Exemplary Claim: 1
DRWN
       46 Drawing Page(s)
LN.CNT 5163
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
      The present invention relates to novel phosphoramidites, including
AB
      positive and neutrally charged compounds. The present invention also
      provides charge tags for attachment to materials including solid
       supports and nucleic acids, wherein the charge tags increase or decrease
      the net charge of the material. The present invention further provides
      methods for separating and characterizing molecules based on the charge
      differentials between modified and unmodified materials.
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L28
    ANSWER 5 OF 16 USPATFULL
AN
       2002:66867 USPATFULL
TI
       Detection of nucleic acid hybridization by
       fluorescence polarization
IN
       Nikiforov, Theo T., San Jose, CA, UNITED STATES
       Jeong, Sang, Mountain View, CA, UNITED STATES
PΙ
       US 2002037520
                         A1
                               20020328
ΑI
       US 2001-854417
                         A1
                               20010511 (9)
      US 2000-203723P
PRAI
                         20000512 (60)
DT
       Utility
```

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FS
       APPLICATION
       LAW OFFICES OF JONATHAN ALAN QUINE, P O BOX 458, ALAMEDA, CA, 94501
LREP
       Number of Claims: 52
CLMN
       Exemplary Claim: 1
ECL
       21 Drawing Page(s)
DRWN
LN.CNT 1793
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Methods, systems and assays are provided for FP detection of
       nucleic acid hybridization.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L28
     ANSWER 6 OF 16 USPATFULL
AN
       2002:34297 USPATFULL
ΤI
       Invasive cleavage of nucleic acids
IN
       Prudent, James R., Madison, WI, United States
       Hall, Jeff G., Madison, WI, United States
       Lyamichev, Victor I., Madison, WI, United States
       Brow, Mary Ann D., Madison, WI, United States
       Dahlberg, James E., Madison, WI, United States
PA
       Third Wave Technologies, Inc., Madison, WI, United States (U.S.
       corporation)
PI
       US 6348314
                               20020219
                          B1
                               19990709 (9)
AΙ
       US 1999-350309
RLI
       Division of Ser. No. US 1996-756386, filed on 29 Nov 1996, now patented,
       Pat. No. US 5985557 Continuation-in-part of Ser. No. US 1996-682853,
       filed on 12 Jul 1996, now patented, Pat. No. US 6001567
       Continuation-in-part of Ser. No. US 1996-599491, filed on 24 Jan 1996,
       now patented, Pat. No. US 5846717, issued on 8 Dec 1998
DT
       Utility
FS
       GRANTED
EXNAM Primary Examiner: Campbell, Eggerton A.
       Medlen & Carroll, LLP
LREP
       Number of Claims: 72
CLMN
ECL
       Exemplary Claim: 1
DRWN
       118 Drawing Figure(s); 90 Drawing Page(s)
LN.CNT 8623
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB
       The present invention relates to means for the detection and
       characterization of nucleic acid sequences, as well
       as variations in nucleic acid sequences. The present
       invention also relates to methods for forming a nucleic
       acid cleavage structure on a target sequence and cleaving the
       nucleic acid cleavage structure in a site-specific
       manner. The structure-specific nuclease activity of a variety of enzymes
       is used to cleave the target-dependent cleavage structure, thereby
       indicating the presence of specific nucleic acid
       sequences or specific variations thereof.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L28 ANSWER 7 OF 16 USPATFULL
AN
       2001:202592 USPATFULL
TI
       Modified ligands of calcium-dependent binding proteins
IN
       Neri, Dario, Zurich, Switzerland
       Winter, Gregory Paul, Cambridge, United Kingdom
PA
       Medical Research Council, London, United Kingdom (non-U.S. corporation)
ΡI
       US 6316409
                         B1 20011113
       WO 9740142 19971030
AΤ
       US 1999-142356
                               19990303 (9)
       WO 1997-GB1152
                               19970425
                               19990303 PCT 371 date
```

09567863 19990303 PCT 102(e) date PRAI GB 1996-8510 19960425 DTUtility FS GRANTED Primary Examiner: Low, Christopher S. F.; Assistant Examiner: Tu, EXNAM LREP Darby & Darby Number of Claims: 19 CLMN Exemplary Claim: 1 ECL 3 Drawing Figure(s); 3 Drawing Page(s) DRWN LN.CNT 814 CAS INDEXING IS AVAILABLE FOR THIS PATENT. The present invention relates to ligands capable of binding a calcium AB dependent binding protein, that comprise an amino acid sequence corresponding to that of a wild type ligand for the calcium dependent binding protein with modification which results in enhanced affinity of the ligand for the calcium dependent binding protein. CAS INDEXING IS AVAILABLE FOR THIS PATENT. ANSWER 8 OF 16 USPATFULL L28 2001:157679 USPATFULL AΝ ΤI Systems for electrophoretic transport and detection of analytes Kayyem, Jon Faiz, Pasadena, CA, United States IN Blackburn, Gary, Glendora, CA, United States O'Connor, Stephen D., Pasadena, CA, United States Clinical Micro Sensors, Inc., Pasadena, CA, United States (U.S. PΑ corporation) PΙ US 6290839 20010918 B1 US 1998-134058 19980814 (9) ΑI US 1998-90389P PRAI 19980623 (60) Utility DTFS GRANTED **EXNAM** Primary Examiner: Tung, T.; Assistant Examiner: Noquerola, Alex Flehr Hohbach Test Albritton & Herbert LLP, Trecartin, Esq., Richard F., LREP Silva, Esq., Robin M. CLMN Number of Claims: 28 ECL Exemplary Claim: 1 DRWN 44 Drawing Figure(s); 21 Drawing Page(s) LN.CNT 4594 CAS INDEXING IS AVAILABLE FOR THIS PATENT. The invention relates to compositions and methods useful in the electrophoretic transport of target analytes to a detection electrode comprising a self-assembled monolayer (SAM). Detection proceeds through the use of an electron transfer moiety (ETM) that is associated with the target analyte, either directly or indirectly, to allow electronic detection of the ETM. CAS INDEXING IS AVAILABLE FOR THIS PATENT. ANSWER 9 OF 16 USPATFULL 2001:116434 USPATFULL AN TI Binding acceleration techniques for the detection of analytes IN Blackburn, Gary, Glendora, CA, United States Creager, Stephen E., Central, SC, United States Fraser, Scott, La Canada, CA, United States Irvine, Bruce D., Glendora, CA, United States

Meade, Thomas J., Altadena, CA, United States O'Connor, Stephen D., Pasadena, CA, United States

Vielmetter, Jost G., Pasadena, CA, United States Welch, Thomas W., Pasadena, CA, United States

Terbrueggen, Robert H., Manhattan Beach, CA, United States

09567863

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Clinical Micro Sensors, Inc., Pasadena, CA, United States (U.S.
PA
       corporation)
                               20010724
       US 6264825
PΙ
                          B1
       US 1999-338726
                               19990623 (9)
ΑI
       Continuation of Ser. No. US 1998-134058, filed on 14 Aug 1998
RLI
PRAI
       US 1998-90389P 19980623 (60)
DT
       Utility
FS
       GRANTED
       Primary Examiner: Tung, T.; Assistant Examiner: Noguerola, Alex
EXNAM
       Flehr Hohabch Test Albritton & Herbert LLP, Trecartin, Esq., Richard F.,
LREP
       Silva, Esq., Robin M.
CLMN
       Number of Claims: 29
       Exemplary Claim: 1
ECL
       49 Drawing Figure(s); 22 Drawing Page(s)
DRWN
LN.CNT 5644
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The invention relates to compositions and methods useful in the
       acceleration of binding of target analytes to capture ligands on
       surfaces. Detection proceeds through the use of an electron transfer
       moiety (ETM) that is associated with the target analyte, either directly
       or indirectly, to allow electronic detection of the ETM.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L28 ANSWER 10 OF 16 USPATFULL
AN
       2000:91761 USPATFULL
ΤI
       Cleavage agents
       Kaiser, Michael W., Madison, WI, United States
TN
       Lyamichev, Victor I., Madison, WI, United States
       Lyamicheva, Natasha, Madison, WI, United States
       Third Wave Technologies, Inc., Madison, WI, United States (U.S.
PA
       corporation)
       US 6090606
                               20000718
PΤ
       US 1996-758314
                               19961202 (8)
ΑI
       Continuation-in-part of Ser. No. US 1996-756386, filed on 26 Nov 1996
RLI
       which is a continuation-in-part of Ser. No. US 1996-682853, filed on 12
       Jul 1996 which is a continuation-in-part of Ser. No. US 1996-599491,
       filed on 24 Jan 1996, now patented, Pat. No. US 5846717 which is a
       continuation-in-part of Ser. No. US 1996-756376, filed on 2 Dec 1996
DT
       Utility
FS
       Granted
EXNAM Primary Examiner: Jones, W. Gary; Assistant Examiner: Shoemaker, Debra
       Medlen & Carroll, LLP
LREP
CLMN
       Number of Claims: 24
       Exemplary Claim: 6
ECL
DRWN
       144 Drawing Figure(s); 117 Drawing Page(s)
LN.CNT 11295
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention relates to means for the detection and
AB
       characterization of nucleic acid sequences, as well
       as variations in nucleic acid sequences. The present
       invention also relates to improved cleavage means for the detection and
       characterization of nucleic acid sequences.
       Structure-specific nucleases derived from a variety of thermostabe
       organisms are provided. These structure-specific nucleases are used to
       cleave target-dependent cleavage structures, thereby indicating the
       presence of specific nucleic acid sequences or
       specific variations thereof.
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L28 ANSWER 11 OF 16 USPATFULL

```
2000:91698 USPATFULL
AN
       Cleavage of nucleic acids
TT
       Prudent, James R., Madison, WI, United States
IN
       Hall, Jeff G., Madison, WI, United States
      Lyamichev, Victor I., Madison, WI, United States
       Brow, Mary Ann D., Madison, WI, United States
       Dahlberg, James E., Madison, WI, United States
       Third Wave Technologies, Inc., Madison, WI, United States (U.S.
PΑ
       corporation)
       US 6090543
                               20000718
PΙ
       US 1996-759038
                               19961202 (8)
AΙ
       Continuation-in-part of Ser. No. US 1996-756386, filed on 26 Nov 1996
RLI
       which is a continuation-in-part of Ser. No. US 1996-682853, filed on 12
       Jul 1996 which is a continuation-in-part of Ser. No. US 1996-599491,
       filed on 24 Jan 1996 76 Ser. No. US 1996-758314, filed on 2 Dec 1996
DT
       Utility
FS
       Granted
      Primary Examiner: Jones, W. Gary; Assistant Examiner: Shoemaker, Debra
EXNAM
       Medlen & Carroll, LLP
LREP
CLMN
       Number of Claims: 27
       Exemplary Claim: 1
ECL
       102 Drawing Figure(s); 117 Drawing Page(s)
DRWN
LN.CNT 11426
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention relates to means for the detection and
       characterization of nucleic acid sequences, as well
       as variations in nucleic acid sequences. The present
       invention also relates to methods for forming a nucleic
       acid cleavage structure on a target sequence and cleaving the
       nucleic acid cleavage structure in a site-specific
       manner. The structure-specific nuclease activity of a variety of enzymes
       is used to cleave the target-dependent cleavage structure, thereby
       indicating the presence of specific nucleic acid
       sequences or specific variations thereof.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L28 ANSWER 12 OF 16 USPATFULL
       1999:163423 USPATFULL
AN
       Detection of nucleic acid sequences by
TI
       invader-directed cleavage
       Brow, Mary Ann D., Madison, WI, United States
TN
       Hall, Jeff Steven Grotelueschen, Madison, WI, United States
       Lyamichev, Victor, Madison, WI, United States
       Olive, David Michael, Madison, WI, United States
       Prudent, James Robert, Madison, WI, United States
       Third Wave Technologies, Inc., CA, United States (U.S. corporation)
PA
PΙ
       US 6001567
                               19991214
ΑI
       US 1996-682853
                               19960712 (8)
RLI
       Continuation-in-part of Ser. No. US 1996-599491, filed on 24 Jan 1996,
       now patented, Pat. No. US 5846717
DT
       Utility
FS
       Granted
EXNAM Primary Examiner: Arthur, Lisa B.; Assistant Examiner: Souaya, Jehanne
LREP
       Medlen & Carroll, LLP
       Number of Claims: 15
CLMN
ECL
       Exemplary Claim: 1
DRWN
       66 Drawing Figure(s); 82 Drawing Page(s)
LN.CNT 7836
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention relates to means for the detection and
AR
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characterization of nucleic acid sequences, as well

as variations in nucleic acid sequences. The present invention also relates to methods for forming a nucleic acid cleavage structure on a target sequence and cleaving the nucleic acid cleavage structure in a site-specific manner. The 5' nuclease activity of a variety of enzymes is used to cleave the target-dependent cleavage structure, thereby indicating the presence of specific nucleic acid sequences or specific variations thereof. The present invention further relates to methods and devices for the separation of nucleic acid molecules based by charge.

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L28 ANSWER 13 OF 16 USPATFULL
       1999:155453 USPATFULL
AN
ΤI
       Detection of nucleic acids by multiple sequential invasive cleavages
       Hall, Jeff G., Madison, WI, United States
ΤN
       Lyamichev, Victor I., Madison, WI, United States
       Mast, Andrea L., Madison, WI, United States
       Brow, Mary Ann D., Madison, WI, United States
PΑ
       Third Wave Technologies, Inc., Madison, WI, United States (U.S.
       corporation)
PΙ
       US 5994069
                               19991130
AΙ
       US 1997-823516
                               19970324 (8)
       Continuation-in-part of Ser. No. WO 1997-US1072, filed on 21 Jan 1997
RLI
       which is a continuation-in-part of Ser. No. US 1996-759038, filed on 2
       Dec 1996 And a continuation-in-part of Ser. No. US 1996-758314, filed on
       2 Dec 1996 which is a continuation-in-part of Ser. No. US 1996-756386,
       filed on 26 Nov 1996 which is a continuation-in-part of Ser. No. US
       1996-682853, filed on 12 Jul 1996 which is a continuation-in-part of
       Ser. No. US 1996-599491, filed on 24 Jan 1996, said Ser. No. US 759038
       which is a continuation-in-part of Ser. No. US 1996-756386, filed on 26
       Nov 1996
       Utility
DT
FS
       Granted
EXNAM Primary Examiner: Jones, W. Gary; Assistant Examiner: Shoemaker, Debra
       Medlen & Carroll, LLP
LREP
       Number of Claims: 34
CLMN
ECL
       Exemplary Claim: 1
DRWN
       169 Drawing Figure(s); 128 Drawing Page(s)
LN.CNT 14892
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AR
       The present invention relates to means for the detection and
       characterization of nucleic acid sequences, as well
       as variations in nucleic acid sequences. The present
       invention also relates to methods for forming a nucleic
       acid cleavage structure on a target sequence and cleaving the
       nucleic acid cleavage structure in a site-specific
       manner. The structure-specific nuclease activity of a variety of enzymes
       is used to cleave the target-dependent cleavage structure, thereby
       indicating the presence of specific nucleic acid
       sequences or specific variations thereof. The present invention further
       relates to methods and devices for the separation of nucleic
       acid molecules based on charge. The present invention also
       provides methods for the detection of non-target cleavage products via
       the formation of a complete and activated protein binding region. The
       invention further provides sensitive and specific methods for the
       detection of human cytomegalovirus nucleic acid in a
       sample.
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ANSWER 14 OF 16 USPATFULL

L28

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1999:146257 USPATFULL
AN
       Invasive cleavage of nucleic acids
TI
IN
       Prudent, James R., Madison, WI, United States
       Hall, Jeff G., Madison, WI, United States
       Lyamichev, Victor I., Madison, WI, United States
       Brow, Mary Ann D., Madison, WI, United States
       Dahlberg, James E., Madison, WI, United States
       Third Wave Technologies, Inc., WI, United States (U.S. corporation)
PA
PΙ
       US 5985557
                               19991116
                               19961126 (8)
ΑI
       US 1996-756386
       Continuation-in-part of Ser. No. US 1996-682853, filed on 12 Jul 1996
RLI
       which is a continuation-in-part of Ser. No. US 1996-599491, filed on 24
       Jan 1996, now patented, Pat. No. US 5846717
\mathbf{DT}
       Utility
       Granted
FS
EXNAM Primary Examiner: Campbell, Eggerton A.
       Medlen & Carroll, LLP
LREP
CLMN
       Number of Claims: 20
       Exemplary Claim: 1
ECL
       87 Drawing Figure(s); 90 Drawing Page(s)
DRWN
LN.CNT 8630
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The present invention relates to means for the detection and
       characterization of nucleic acid sequences, as well
       as variations in nucleic acid sequences. The present
       invention also relates to methods for forming a nucleic
       acid cleavage structure on a target sequence and cleaving the
       nucleic acid cleavage structure in a site-specific
       manner. The structure-specific nuclease activity of a variety of enzymes
       is used to cleave the target-dependent cleavage structure, thereby
       indicating the presence of specific nucleic acid
       sequences or specific variations thereof.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
    ANSWER 15 OF 16 USPATFULL
L28
       1998:17197 USPATFULL
AN
       Labeled complex and method of analysis therewith
ΤI
       Miyazaki, Takeshi, Ebina, Japan
IN
       Okamoto, Tadashi, Yokohama, Japan
       Tanaka, Kazumi, Yokohama, Japan
       Onishi, Toshikazu, Machida, Japan
       Fukui, Tetsuro, Yokohama, Japan
       Yamamoto, Nobuko, Isehara, Japan
PΑ
       Canon Kabushiki Kaisha, Tokyo, Japan (non-U.S. corporation)
PΙ
       US 5719027
                               19980217
ΑI
       US 1996-605624
                               19960222 (8)
       Division of Ser. No. US 1994-191931, filed on 4 Feb 1994, now abandoned
RLI
PRAI
       JP 1993-19057
                           19930205
DT
       Utility
       Granted
EXNAM Primary Examiner: Green, Lora M.
LREP
       Fitzpatrick, Cella, Harper & Scinto
CLMN
       Number of Claims: 7
ECL
       Exemplary Claim: 1
       3 Drawing Figure(s); 3 Drawing Page(s)
DRWN
LN.CNT 915
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       A labeled complex formed by combining a labeling agent with a biological
       substance, where the labeling agent is a trinucleus dye represented by
       the general formula (I)' or (II)':
```

```
ring(Xa)-La-ring(Xb)-Lb-ring(Xc)
```

(I)

[ring(Xa)-La-ring(Xb)-Lb-ring(Xc)].sup..sym. Y.sup..crclbar.(II)'

where the ring(Xa), ring(Xb), and ring(Xc), which mean rings having Xa, Xb; or Xc respectively, are independently a heterocyclic ring having one to three heteroatoms of oxygen, sulfur, nitrogen, or selenium, the heterocyclic ring being unsubstituted or substituted by any of a substituted or unsubstituted alkyl group, a substituted or unsubstituted aryl group, and a substituted or unsubstituted aralkyl group; La and Lb are independently a methine chain composed of one to six substituted or unsubstituted methine linkage, and one of La and Lb may be omitted to link directly the heterocyclic rings; and Y.sup..crclbar. represents an anion.

A method of analysis, comprises combining any of the labeled complex with a target substance to be detected, and detecting the target substance optically.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

```
L28 ANSWER 16 OF 16 · USPATFULL
       96:80407 USPATFULL
AN
       Haptenic probes for detecting capture polynucleotides
TI
       Adams, Craig W., Corona, CA, United States
ΙN
       Beckman Instruments, Inc., Fullerton, CA, United States (U.S.
PA
       corporation)
                               19960903
       US 5552541
PΙ
       US 1990-541143
                               19900620 (7)
ΑI
DT
       Utility
FS
       Granted
EXNAM Primary Examiner: Jones, W. Gary; Assistant Examiner: Marschel, Ardin H.
      May, William H., Henry, Janis C.
LREP
CLMN
       Number of Claims: 7
ECL
       Exemplary Claim: 1
DRWN
       9 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 1552
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Nucleic acid probes and protein probes are
       disclosed. The nucleic acid probe comprises a probe
       polynucleotide, a charged hapten label, and a binding moiety. The
       protein probe comprises a probe protein, a charged hapten label and a
       binding moiety. The charged hapten label joint to the binding moiety can
       comprise a negatively charged sulfophenylhydrazine tag compound.
       Polyclonal antibodies and monoclonal antibodies with specific affinity
       for the charged hapten labels are disclosed as are hybridomas capable of
       making the monoclonal antibodies. Methods and kits are disclosed for
       making the nucleic acid probes, making the protein
       probes, detecting a capture polynucleotide of the nucleic
       acid probe and detecting a capture molecule of the protein
       probe.
```

```
=> d 128 16 kwic
```

```
L28 ANSWER 16 OF 16 USPATFULL

AB Nucleic acid probes and protein probes are
disclosed. The nucleic acid probe comprises a probe
polynucleotide, a charged hapten label, and a binding moiety. The
```

- protein probe comprises a probe protein, . . . labels are disclosed as are hybridomas capable of making the monoclonal antibodies. Methods and kits are disclosed for making the nucleic acid probes, making the protein probes, detecting a capture polynucleotide of the nucleic acid probe and detecting a capture molecule of the protein probe.
- SUMM The present invention is directed to novel nucleic acid probes and protein probes. The invention is also directed to particular novel polyclonal and monoclonal antibodies useful for detecting the. . .
- SUMM Nucleic acid probes, also called hybridization probes, allow specific polynucleotide sequences to be detected. Protein probes make possible detection of various compounds,. . .
- SUMM Nucleic acid probes can be used to detect specific polynucleotide sequences and can assist the diagnosis and treatment of numerous genetic disorders. . .
- SUMM Nucleic acid probes can also reveal genes coding antigens responsible for graft rejection. Genetic information useful in cancer oncogeny testing and forensic. . .
- SUMM . . . I autoradiography. Furthermore, the .sup.32 P isotope is a hazardous isotope. Hence, there is a need for nonradioactive labels for nucleic acid and protein probes.
- SUMM . . . time, a "stickiness" or aggregation problem is encountered with biotin labels. Stickiness refers to the situation wherein biotinylated antibodies and/or nucleic acid probes aggregate due to the change in the surface characteristics of normally charged polynucleotides conjugated to neutral (uncharged) biotin. The. . .
- SUMM . . . been sought for incorporation into probes to address these problems. The nonradioactive label can also be useful as an alternate nucleic acid and protein probe label. When biotin alternative labels are used in conjunction with biotinylated probes, sandwich assays can be performed. . .
- SUMM The term "polynucleotide" is used interchangeably with the term " nucleic acid" and includes all oligonucleotides.
- SUMM . . . is a 4-hydrazinobenzenesulfonate anion compound covalently attached through its hydrazine terminus to the 4-position of a cytosine base of single-stranded nucleic acid. This nucleic acid probe can be made under mild conditions and its use allows detection of picogram amounts of capture polynucleotide.
- SUMM The present invention satisfies the prior-art need for a nucleic acid label and a protein probe label that, when joined to a binding moiety, is soluble, stable, reactive, haptenic, nonradioactive and. . .
- DRWD . . . the results of in situ detection of HPV 6 DNA in a human cervical biopsy tissue specimen using a sulfophenyl-labeled nucleic acid probe.
- DETD . . . that certain compounds can function as superior nonradioactive haptenic labels for labeling polynucleotides. The labeled polynucleotides can be used as nucleic acid probes.

 Nucleic acid probes, or hybridization probes as they are also called, can be used to detect specific polynucleotide sequences. Specific polynucleotide sequences. . .
- DETD The probe polynucleotide can be DNA or RNA and is preferably a single-stranded nucleic acid. The attaching reaction whereby the label is attached to the probe polynucleotide is more difficult with a double-stranded nucleic acid.
- DETD . . . negatively charged. A negative charge has been found to help reduce the "stickiness" or aggregation problem encountered with neutral or **positively charged labels**. A preferred label is a haptenic, anionic sulfophenyl compound, commercially available and generally stable at room temperature.

```
. . . can be, for example, an antibody, antigen, hormone, steroid,
DETD
       carbohydrate, enzyme inhibitor, enzyme effector, various enzyme
       substrate analogues, and a nucleic acid.
       A hybridization probe was made by attaching sulfophenylhydrazine to a
DETD
       cytosine base-containing nucleic acid in an
       attaching reaction. The sulfophenylhydrazine was used in a labeling mix.
       The reagents used to prepare the labeling mix.
             . supernatant contains antisulfophenyl antibody conjugated to
DETD
       alkaline phosphatase. This complex can be used to detect the sulfophenyl
       label of a nucleic acid probe or of a protein probe.
       Improved detection of smaller amounts of sulfophenyl label can be
       possible because the enzyme.
DETD
                methods that can be used to detect a capture polynucleotide or
       capture molecule that has reacted with, respectively, a
       sulfophenyl-labeled nucleic acid probe or a
       sulfophenyl-labeled protein probe. Enzymes, enzyme conjugates, haptens,
       and nonhaptenic labels different from those set forth but known.
DETD
       Nucleic acid probes and protein probes according to
       the present invention have many advantages including the following:
       4. No purification of the nucleic acid is required
DETD
       before the nucleic acid is labeled.
=> s positiv? (a) charg? phosphoramidite
             2 POSITIV? (A) CHARG? PHOSPHORAMIDITE
=> d 130 bib abs 1-2
L30 ANSWER 1 OF 2 WPIDS (C) 2002 THOMSON DERWENT
ΔN
     2002-674850 [72]
                        WPIDS
     1997-393613 [36]
CR
DNC C2002-190055
     Composition useful for e.g. separation of nucleic acids comprises a
TI
     positively or neutrally charged phosphoramidite.
DC
     B04 B05 D16
IN
     ALLAWI, H T; LYAMICHEV, V; NERI, B P; SKRZPCZYNSKI, Z; TAKOVA, T; WAYLAND,
PΑ
     (THIR-N) THIRD WAVE TECHNOLOGIES INC
CYC 100
PΙ
     WO 2002063030 A2 20020815 (200272)* EN 197p
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TR TZ UG ZM ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
            KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
            RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM
            ZW
     US 2002128465 A1 20020912 (200272)
     WO 2002063030 A2 WO 2002-US3423 20020206; US 2002128465 A1 CIP of US
ADT
     1996-682853 19960712, CIP of US 1999-333145 19990614, US 2001-777430
     20010206
FDT US 2002128465 A1 CIP of US 6001567
PRAI US 2001-777430
                      20010206; US 1996-682853 19960712; US 1999-333145
     19990614
AN
     2002-674850 [72]
                        WPIDS
CR
     1997-393613 [36]
AB
     WO 200263030 A UPAB: 20021108
     NOVELTY - Composition comprises a positively or neutrally charged
     phosphoramidite.
          DETAILED DESCRIPTION - Composition (c) or (c') comprises a
     positively charged phosphoramidite of formula
     (I) or a neutrally charged phosphoramidite of formula (II). (I) comprises
```

nitrogen-containing chemical group selected from primary, secondary or tertiary amine or ammonium group. (II) comprises secondary or tertiary amine or ammonium group.

X, Z = a reactive phosphate group;

Y = a protected hydroxy group;

X' = a protected hydroxy group;

N, N' = an amine group.

INDEPENDENT CLAIMS are included for the following:

- (1) a composition (c1) comprising a charge tag (x1) attached to a terminal end of a nucleic acid molecule, the charge tag comprises a phosphate group and a positively charged molecule;
- (2) a composition (c2) comprising a nucleic acid molecule that comprises a positively charged phosphoramidite
- (3) a composition (c3) comprising a charge tag attached to the terminal end of a nucleic acid molecule, the charge tag comprises a positively charged phosphoramidite;
- (4) a composition (c4) comprising a fluorescent dye directly bonded to a phosphate group, which is not directly bonded to an amine group;
- (5) a mixture (m) comprising a number of oligonucleotides, each oligonucleotide is attached to a different charge tag with each charge tag comprising a phosphate group and a positively charged group;
- (6) a composition (c5) comprising a solid support attached to a charged tag, the charge tag comprises a positively charged group and a reactive group configured to allow the charge tag to covalently attach to the nucleic acid molecule;
 - (7) separating nucleic acid molecules involving either:
- (a) treating (m1) a charge-balanced oligonucleotide containing the charge tag to produce a charge-unbalanced oligonucleotide and separating the charge-unbalanced oligonucleotide from the reaction mixture; or
- (b) treating (m2) a number of charge-balanced oligonucleotides, each containing different charge tags, to produce at least 2 charge-unbalanced oligonucleotides, and separating the charge-unbalanced oligonucleotides from the reaction mixture.
- USE The composition is useful for separation of nucleic acid molecules (claimed). The composition is further useful for fractionation of specific nucleic acids by selective charge reversal useful in e.g. INVADER assay cleavage reactions; and in the synthesis of charge-balanced molecules.

ADVANTAGE - In the fractionation of nucleic acid molecules, the method provides an absolute readout of the partition of products from substrates (i.e. provides a 100% separation). Through the use of multiple positively charged adducts, synthetic molecules can be constructed with sufficient modification due to the fact that the normally negatively charged strand is made nearly neutral. It is also possible to distinguish between a enzymatically or thermally degraded DNA fragments due to the absence or presence of 3'phosphate.

Dwg.0/46

```
L30 ANSWER 2 OF 2 USPATFULL AN 2002:236261 USPATFULL
       Charge tags and the separation of nucleic acid molecules
TI
IN
       Lyamichev, Victor, Madison, WI, UNITED STATES
       Skrzpczynski, Zbigniew, Verona, WI, UNITED STATES
       Allawi, Hatim T., Madison, WI, UNITED STATES
       Wayland, Sarah R., Madison, WI, UNITED STATES
       Takova, Tsetska, Madison, WI, UNITED STATES
       Neri, Bruce P., Madison, WI, UNITED STATES
PA
       Third Wave Technologies, Inc. (U.S. corporation)
PΙ
       US 2002128465
                           A1
                                20020912
ΑI
       US 2001-777430
                           A1
                                 20010206 (9)
       Continuation-in-part of Ser. No. US 1999-333145, filed on 14 Jun 1999,
RLI
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09567863

PENDING Continuation-in-part of Ser. No. US 1996-682853, filed on 12 Jul 1996, GRANTED, Pat. No. US 6001567 DTUtility FS APPLICATION MEDLEN & CARROLL, LLP, 101 HOWARD STREET, SUITE 350, SAN FRANCISCO, CA, LREP CLMN Number of Claims: 86 Exemplary Claim: 1 ECL 46 Drawing Page(s) DRWN LN.CNT 5163 CAS INDEXING IS AVAILABLE FOR THIS PATENT. The present invention relates to novel phosphoramidites, including positive and neutrally charged compounds. The present invention also provides charge tags for attachment to materials including solid supports and nucleic acids, wherein the charge tags increase or decrease the net charge of the material. The present invention further provides methods for separating and characterizing molecules based on the charge differentials between modified and unmodified materials. CAS INDEXING IS AVAILABLE FOR THIS PATENT. => d his (FILE 'HOME' ENTERED AT 10:12:59 ON 18 DEC 2002) FILE 'BIOSIS, MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 10:13:34 ON 18 DEC 2002 343861 S NUCLEIC ACID L1L22 S L1 AND POSITIV? (3A) CHARGE TAG (3A) NUCLEIC ACID? 21 S L1 AND POSITIV? (4A) CHARG? (3A) TAG? L3 19 S L3 NOT L2 L419 DUP REM L4 (0 DUPLICATES REMOVED) L5109 S L1 AND POSITIV? (4A) LABEL L6 108 S L6 NOT L5 L792 S L7 AND PHOSPHAT? L8L9 92 DUP REM L8 (0 DUPLICATES REMOVED) 22 S L9 AND POSITIV? (4A) CHARG? L101 S POSITIV? (3A) CHARG? (3A) LABEL? (4A) TERMINAL (4A) (NUCLEIC L111 S L11 AND POSITIV? L12110 S MASS TAG L13 L1450 S L13 AND OLIGONUCLEOTIDE? 43 S L14 AND LABEL? L15 L16 21 S L15 AND TERMINAL L17 21 DUP REM L16 (0 DUPLICATES REMOVED) L18 1 S POSITIV? CHARG? LABEL? OLIGONUCLEOTIDE? 1 S POSITIV? (4A) CHARG? LABEL? (3A) OLIGONUCLEOTIDE? L19 L20 117 S POSITIV? (5A) (LABEL? OR TAG?) (4A) OLIGONUCLEOTIDE? L21 31 S L20 AND AMINE L22 23 S L21 AND AMMONIUM L23 2 S L22 AND PHOSPHORAMIDITE L2421 S L22 NOT L23 L25 25 S POSITIV? (3A) CHARG? (3A) PHOSPHORAMIDITE? 25 DUP REM L25 (0 DUPLICATES REMOVED) L26 L27 21 S POSITIV? CHARG? LABEL? L28 16 S L27 AND NUCLEIC ACID 1 S L28 AND POSITIV? (2A) PHOSPHORAMIDITE L29 L30 2 S POSITIV? (A) CHARG? PHOSPHORAMIDITE

=>

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=>
=> s 132 and charq?
             9 L32 AND CHARG?
=> d 133 bib abs 1-9
L33 ANSWER 1 OF 9 WPIDS (C) 2002 THOMSON DERWENT
    2002-706900 [76]
AN
                       WPIDS
DNC C2002-200480
    Preparation of oligonucleotides used as diagnostic agents, research
ΤI
     reagents and therapeutics comprises reacting nucleoside
    phosphoramidite with a support bound oligomer in presence of
     neutralizing agent.
DC
    B03 B04
    GUZAEV, A P; MANOHARAN, M
IN
PA
    (GUZA-I) GUZAEV A P; (MANO-I) MANOHARAN M; (ISIS-N) ISIS PHARM INC
CYC 98
PΙ
    WO 2002062811 A2 20020815 (200276)* EN
                                              92p
       RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
           NL OA PT SD SE SL SZ TR TZ UG ZM ZW
        W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
           DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
           KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PL PT RO
           RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZM ZW
     US 2002147331 A1 20021010 (200276)
    WO 2002062811 A2 WO 2002-US2336 20020128; US 2002147331 A1 US 2001-775967
ADT
     20010202
PRAI US 2001-775967
                     20010202
    2002-706900 [76]
AN
                       WPIDS
AΒ
     WO 200262811 A UPAB: 20021125
    NOVELTY - Preparation of oligonucleotides comprises reacting a nucleoside
     phosphoramidite with a support bound oligomer having at least one
     unprotected internucleoside linkage in the presence of a neutralizing
     agent (A) comprising e.g. aliphatic amine, aliphatic
    heterocyclic amine or aromatic amine.
         DETAILED DESCRIPTION - Preparation of oligonucleotides comprises
     reacting a nucleoside phosphoramidite with a support bound oligomer having
     at least one unprotected internucleoside linkage comprising a phosphate
     linkage, phosphorothioate linkage or phosphorodithioate linkage, in the
    presence of a neutralizing agent comprising an aliphatic amine,
     aliphatic heterocyclic amine, aromatic amine, aromatic
    heterocyclic amine, guanidine or a salt of formula D+E-.
         D+ = quaternary tetraalkylammonium cation or a protonated aliphatic
     amine, aliphatic heterocyclic amine, aromatic
     amine, aromatic heterocyclic amine or guanidine, and
         E- = tetrazolide anion, 4,5-dicyanoimidazolide anion, optionally
     substituted alkylsulfonate anion, optionally substituted arylsulfonate
     anion, tetrafluoroborate anion, hexafluorophosphate anion or
     trihaloacetate anion.
          INDEPENDENT CLAIMS are included for the following:
          (1) forming an internucleoside linkage which comprises reacting a
    phosphoramidite of formula (I) with a compound of formula (II) in the
    presence of (A);
          (2) a method which comprises deprotecting the 5'-hydroxyl group of a
    solid support having a 5'-O-protected phosphorus-linked oligomer having at
    least one phosphoryl internucleoside linkage that does not have a
    phosphoryl protecting group, washing with a solution containing (A),
    reacting the free hydroxyl with a 5'-protected nucleoside phosphoramidite
    to form a phosphite triester linkage and oxidizing or sulfurizing the
    covalent linkage to form a phosphodiester, phosphorothioate,
    phosphorodithioate or H-phosphonate linkage, and
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AN

CR

TI

DC

IN

PA CYC

PΙ

FDT

AN

CR

AΒ

```
(3) a composition comprising a 5'-protected nucleoside
     phosphoramidite and D+E-.
          L1 = an internucleoside linkage;
     n1 = 0-100;
          R1 = OH protecting group;
          R2 = 2'-substituent group;
          R4, R5 = 1-10C alkyl or
          NR4R5 = heterocyclyl;
          B = a nucleobase;
          Q, Z, X = 0 \text{ or } S;
          Pg = phosphoryl protecting group;
          R3 = a linker connected to a solid support;
     n = 1-100;
          L = O-P(=X)(-Z-Y)-O, and
          Y = phosphoryl protecting group or a negative charge,
     provided that at least one is a negative charge.
          ACTIVITY - None given in the source material.
          MECHANISM OF ACTION - Transcription factor inhibitor; Gene therapy.
          USE - Useful as diagnostic reagents, research reagents and
     therapeutics for modulating the action of transcriptase factors.
          ADVANTAGE - The method avoids the need for phosphoryl protecting
     groups.
     Dwg.0/22
L33 ANSWER 2 OF 9 WPIDS (C) 2002 THOMSON DERWENT
     2002-674850 [72]
                        WPIDS
     1997-393613 [36]
DNC C2002-190055
     Composition useful for e.g. separation of nucleic acids comprises a
     positively or neutrally charged phosphoramidite.
     B04 B05 D16
     ALLAWI, H T; LYAMICHEV, V; NERI, B P; SKRZPCZYNSKI, Z; TAKOVA, T; WAYLAND,
     (THIR-N) THIRD WAVE TECHNOLOGIES INC
    100
     WO 2002063030 A2 20020815 (200272)* EN 197p
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TR TZ UG ZM ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
            KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
            RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM
            ZW
     US 2002128465 A1 20020912 (200272)
    WO 2002063030 A2 WO 2002-US3423 20020206; US 2002128465 A1 CIP of US
     1996-682853 19960712, CIP of US 1999-333145 19990614, US 2001-777430
     20010206
    US 2002128465 A1 CIP of US 6001567
PRAI US 2001-777430 20010206; US 1996-682853 19960712; US 1999-333145
     19990614
     2002-674850 [72]
     1997-393613 [36]
     WO 200263030 A UPAB: 20021108
     NOVELTY - Composition comprises a positively or neutrally charged
     phosphoramidite.
          DETAILED DESCRIPTION - Composition (c) or (c') comprises a positively
     charged phosphoramidite of formula (I) or a neutrally
     charged phosphoramidite of formula (II). (I) comprises
     nitrogen-containing chemical group selected from primary, secondary or
     tertiary amine or ammonium group. (II) comprises secondary or
     tertiary amine or ammonium group.
          X, Z = a reactive phosphate group;
```

- Y = a protected hydroxy group;
- X' = a protected hydroxy group;
- N, N' = an amine group.

INDEPENDENT CLAIMS are included for the following:

- (1) a composition (c1) comprising a **charge** tag (x1) attached to a terminal end of a nucleic acid molecule, the **charge** tag comprises a phosphate group and a positively **charged** molecule;
- (2) a composition (c2) comprising a nucleic acid molecule that comprises a positively **charged** phosphoramidite;
- (3) a composition (c3) comprising a **charge** tag attached to the terminal end of a nucleic acid molecule, the **charge** tag comprises a positively **charged** phosphoramidite;
- (4) a composition (c4) comprising a fluorescent dye directly bonded to a phosphate group, which is not directly bonded to an **amine** group;
- (5) a mixture (m) comprising a number of oligonucleotides, each oligonucleotide is attached to a different **charge** tag with each **charge** tag comprising a phosphate group and a positively **charged** group;
- (6) a composition (c5) comprising a solid support attached to a charged tag, the charge tag comprises a positively charged group and a reactive group configured to allow the charge tag to covalently attach to the nucleic acid molecule;
 - (7) separating nucleic acid molecules involving either:
- (a) treating (m1) a charge-balanced oligonucleotide containing the charge tag to produce a charge -unbalanced oligonucleotide and separating the charge-unbalanced oligonucleotide from the reaction mixture; or
- (b) treating (m2) a number of **charge**-balanced oligonucleotides, each containing different **charge** tags, to produce at least 2 **charge**-unbalanced oligonucleotides, and separating the **charge**-unbalanced oligonucleotides from the reaction mixture.
- USE The composition is useful for separation of nucleic acid molecules (claimed). The composition is further useful for fractionation of specific nucleic acids by selective **charge** reversal useful in e.g. INVADER assay cleavage reactions; and in the synthesis of **charge**-balanced molecules.

ADVANTAGE - In the fractionation of nucleic acid molecules, the method provides an absolute readout of the partition of products from substrates (i.e. provides a 100% separation). Through the use of multiple positively charged adducts, synthetic molecules can be constructed with sufficient modification due to the fact that the normally negatively charged strand is made nearly neutral. It is also possible to distinguish between a enzymatically or thermally degraded DNA fragments due to the absence or presence of 3'phosphate.

Dwg.0/46

- L33 ANSWER 3 OF 9 USPATFULL
- AN 1999:13039 USPATFULL
- TI **Phosphoramidite** derivatives, their preparation and the use thereof in the incorporation of reporter groups on synthetic oligonucleotides
- IN Misiura, Konrad, Lodz, Poland
 - Gait, Michael J., Cambridge, Great Britain
- PA Amersham International plc, Buckinghamshire, England (non-U.S. corporation)
- PI US 5864032 19990126
- AI US 1995-406700 19950320 (8)
- RLI Division of Ser. No. US 1992-946477, filed on 3 Nov 1992, now patented, Pat. No. US 5567811

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PRAI
       GB 1990-9980
                            19900503
DT
       Utility
FS
       Granted
EXNAM
       Primary Examiner: Elliott, George G.; Assistant Examiner: Houtteman,
       Scott W.
LREP
       Wenderoth, Lind & Ponack
CLMN
       Number of Claims: 6
ECL
       Exemplary Claim: 1
DRWN
       11 Drawing Figure(s); 9 Drawing Page(s)
LN.CNT 1119
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Phosphoramidite derivatives of formula (V), ##STR1## wherein X is biotin
AB
       and Y is a protecting group. There may be a linker arm, of variable
       length, between X and the rest of the molecule. Examples of the
       protecting group Y include 4,4'-dimethoxytrityl, trifluoroacetyl and
       fluorenylmethoxycarbonyl (Fmoc). The phosphoramidite derivatives are
       useful in single or multiple labelling of synthetic oligonucleotides.
       Process for the preparation of these phosphoramidite derivatives are
       also disclosed.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 4 OF 9 USPATFULL
L33
       1998:144261 USPATFULL
ΔN
TΤ
       Phosphoramidite derivatives of macrocycles
IN
       Magda, Darren, Cupertino, CA, United States
       Sessler, Jonathan L., Austin, TX, United States
       Crofts, Shaun P., Campbell, CA, United States
Board of Regents, The University of Texas, Austin, TX, United States
PA
       (U.S. corporation)
       Pharmacyclics, Inc., Sunnyvale, CA, United States (U.S. corporation)
       US 5837866
PΤ
                                19981117
AΙ
       US 1997-862778
                                19970523 (8)
       Continuation-in-part of Ser. No. US 1996-614638, filed on 13 Mar 1996,
RLI
       now patented, Pat. No. US 5633354 which is a continuation of Ser. No. US
       1995-487722, filed on 7 Jun 1995, now patented, Pat. No. US 5565552
       which is a continuation-in-part of Ser. No. US 1994-310501, filed on 21
       Sep 1994, now patented, Pat. No. US 5567587
DT
       Utility
FS
       Granted
EXNAM
       Primary Examiner: Raymond, Richard L.
LREP
       Larson, Jacqueline S.
CLMN
       Number of Claims: 12
ECL
       Exemplary Claim: 1
DRWN
       8 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 1195
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The invention is directed to phosphoramidite derivatives of macrocycles,
       such as porphyrins and expanded porphyrins, including sapphyrins and
       texaphyrins. The phosphoramidite derivatives are useful as intermediates
       in the preparation of macrocycle-oligonucleotide conjugates.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
     ANSWER 5 OF 9 USPATFULL
L33
       97:45114 USPATFULL
AN
ΤI
       Phosphoramidite derivatives of texaphyrins
IN
       Magda, Darren, Cupertino, CA, United States
       Sessler, Jonathan L., Austin, TX, United States
       Iverson, Brent L., Austin, TX, United States
       Sansom, Petra I., Austin, TX, United States
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Crofts, Shaun P., Campbell, CA, United States

also disclosed.

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Pharmacyclics, Inc., Sunnyvale, CA, United States (U.S. corporation)
PΑ
       Board of Regents, The University of Texas, Austin, TX, United States
       (U.S. corporation)
       US 5633354
                               19970527
PΤ
                               19960313 (8)
ΔΤ
       US 1996-614638
       Continuation of Ser. No. US 1995-487722, filed on 7 Jun 1995, now
RLI
       patented, Pat. No. US 5565552 which is a continuation-in-part of Ser.
       No. US 1994-310501, filed on 21 Sep 1994, now patented, Pat. No. US
       5567687
       Utility
DT
       Granted
FS
EXNAM Primary Examiner: Raymond, Richard L.
      Larson, Jacqueline S.
LREP
      Number of Claims: 18
CLMN
       Exemplary Claim: 1
ECL
       7 Drawing Figure(s); 7 Drawing Page(s)
DRWN
LN.CNT 996
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       The invention is directed to a method of incorporating expanded
AB
       porphyrins, and particularly of incorporating a sapphyrin or a
       texaphyrin, before, during, or after chemical synthesis of an oligomer
       to form an expanded porphyrin-oligonucleotide conjugate, and
       particularly a sapphyrin- or texaphyrin-oligonucleotide conjugate. This
       method includes reacting derivatized nucleotides and a sapphyrin or a
       texaphyrin in a desired order in an automated or manual DNA synthesizer
       having a solid support to form a sapphyrin- or a texaphyrin-
       oligonucleotide conjugate.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
    ANSWER 6 OF 9 USPATFULL
L33
       96:97145 USPATFULL
AN
ΤI
       Phosphoramidite derivatives, their preparation and the use
       thereof in the incorporation of reporter groups on synthetic
       oligonucleotides
       Misiura, Konrad, Lodz, Poland
IN
       Gait, Michael, Cambridge, Great Britain
PA
       Amersham International plc, England (non-U.S. corporation)
       US 5567811
                               19961022
PΙ
       WO 9117169 19911114
       US 1992-946477
                               19921103 (7)
ΑI
       WO 1991-GB713
                               19910503
                               19921103 PCT 371 date
                               19921103 PCT 102(e) date
PRAI
      GB 1990-9980
                           19900503
      Utility
DT
FS
       Granted
EXNAM Primary Examiner: Jones, W. Gary; Assistant Examiner: Houtteman, Scott
LREP
      Wenderoth, Lind & Ponack
      Number of Claims: 6
CLMN
       Exemplary Claim: 1
ECL
       11 Drawing Figure(s); 9 Drawing Page(s)
LN.CNT 1128
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Phosphoramidite derivatives of formula (V), ##STR1## wherein X is biotin
AB
       and Y is a protecting group. There may be a linker arm, of variable
       length, between X and the rest of the molecule. Examples of the
       protecting group Y include 4,4'-dimethoxytrityl, trifluoroacetyl and
       fluorenylmethoxycarbonyl (Fmoc). The phosphoramidite derivatives are
       useful in single or multiple labelling of synthetic oligonucleotides.
       Process for the preparation of these phosphoramidite derivatives are
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L33 ANSWER 7 OF 9 USPATFULL
       91:50608 USPATFULL
AN
       Phosphoramidite compounds and process for production thereof
TΙ
IN
       Nojiri, Ryuji, Aichi, Japan
       Hayakawa, Yoshihiro, Ichinomiya, Japan
       Uchiyama, Mamoru, Kawasaki, Japan
       Kato, Hisatoyo, Ohbu, Japan
       Chino, Yasuyoshi, Tokyo, Japan
       Tahara, Shinichiro, Yokohama, Japan
       Nippon Zeon Co., Ltd., Tokyo, Japan (non-U.S. corporation)
PA
                               19910625
PΙ
       US 5026838
                               19880804 (7)
       US 1988-229773
ΑI
       Continuation of Ser. No. US 1986-909728, filed on 22 Sep 1986, now
RLI
       abandoned
       JP 1985-211240
                           19850925
PRAI
       JP 1985-223138
                           19851007
DT
       Utility
       Granted
FS
      Primary Examiner: Brown, Johnnie R.; Assistant Examiner: Crane, L. Eric
EXNAM
LREP
       Sherman & Shalloway
      Number of Claims: 14
CLMN
ECL
       Exemplary Claim: 1
DRWN
       No Drawings
LN.CNT 855
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
       Phosphoramidite compounds of the general formula ##STR1## wherein each
AΒ
       of R.sub.1 and R.sub.2 represents a hydroxyl group having a protective
       group, or the group --OR.sub.4, R.sub.3 represents a hydrogen atom, a
       hydroxyl group having a protective group, or the group -- OR. sub. 4,
       R.sub.4 represents the group ##STR2## X represents a secondary amino
       group, R.sub.5 represents an allylic residue or a protective group
       capable of being split off by beta-cleavage, and B.sup.AOC represents a
       nucleoside base residue in which the amino or imino group is protected
       with an allyloxycarbonyl-type residue, with the proviso that only one of
       R.sub.1, R.sub.2 and R.sub.3 represents the group--OR.sub.4. The
       compounds can be produced by reacting a nucleoside represented by the
       general formula ##STR3## wherein each of R.sub.1 ' and R.sub.2
       represents a hydroxyl group which may have a protective group, R.sub.3 '
       represents a hydrogen atom, or a hydroxyl group which may have a
       protective group, and B.sup.AOC is as defined, with the proviso that
       only one of R.sub.1 ', R.sub.2 'and R.sub.3 ' is a hydroxyl group,
       with a phosphoramide compound represented by the general formula
       ##STR4## wherein X and R.sub.5 are as defined, and Y represents a
       secondary amino group or a halogen atom.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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L33 ANSWER 8 OF 9 USPATFULL
AN
       87:38081 USPATFULL
TI
       Phosphoramidite nucleoside compounds
IN
       Caruthers, Marvin H., Boulder, CO, United States
       Beaucage, Serge L., Mountain View, CA, United States
       University Patents, Inc., Westport, CT, United States (U.S. corporation)
PA
PΙ
                               19870526
      US 4668777
ΑI
      US 1984-637927
                               19840806 (6)
DCD
      20001115
       Continuation of Ser. No. US 1982-358589, filed on 16 Mar 1982, now
RLI
       abandoned which is a continuation-in-part of Ser. No. US 1981-248450,
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09567863

filed on 27 Mar 1981, now patented, Pat. No. US 4415732 Utility DT FS Granted EXNAM Primary Examiner: Brown, Johnnie R.; Assistant Examiner: Peselev, Elli Yahwak, George M. LREP Number of Claims: 25 CLMN ECL Exemplary Claim: 1 No Drawings DRWN LN.CNT 1059 CAS INDEXING IS AVAILABLE FOR THIS PATENT. AB A new class of nucleoside phosphoramidites which are relatively stable to permit isolation thereof and storage at room temperature. The phosphoramidites are derivatives of saturated secondary amines. CAS INDEXING IS AVAILABLE FOR THIS PATENT. L33 ANSWER 9 OF 9 USPATFULL AN83:53604 USPATFULL TT Phosphoramidite compounds and processes IN Caruthers, Marvin H., Boulder, CO, United States Beaucage, Serge L., Boulder, CO, United States University Patents, Inc., Norwalk, CT, United States (U.S. corporation) PA US 4415732 PΙ 19831115 US 1981-248450 AΙ 19810327 (6) DT Utility FS Granted EXNAM Primary Examiner: Love, Ethel G. Scully, Scott, Murphy & Presser LREP Number of Claims: 20 CLMNECLExemplary Claim: 1 DRWN No Drawings LN.CNT 553 CAS INDEXING IS AVAILABLE FOR THIS PATENT. A new class of nucleoside phosphoramidites which are relatively stable to permit isolation thereof and storage at room temperature. The phosphoramidites are derivatives of saturated secondary amines. CAS INDEXING IS AVAILABLE FOR THIS PATENT. => d 133 9 kwic L33 ANSWER 9 OF 9 USPATFULL Phosphoramidite compounds and processes SUMM . . heteroatoms such as N, S or O. These compounds of structure II and IIa wherein X is such a heterocyclic amine, i.e., one in which the amino nitrogen is a ring heteroatom, are characterized by an extremely high reactivity, and consequently. . . . compounds of the present invention can be prepared according to SUMM art-recognized procedures such as by reaction of the selected secondary amine with the corresponding nucleoside phosphomonochloridite. This reaction is accomplished by dissolving the said nucleoside in an organic solvent, such as tetrahydrofuran or acetonitrile, and adding the selected secondary amine. After removing unwanted hydrochloride salt, the organic solvent solution of the phosphoramidite may be used as such for polynucleotide synthesis. SUMM . . . chloro-(2.degree. amino)alkyoxyphosphine is effected in an organic solvent solution of the selected nucleoside, preferably in the presence of a tertiary amine to take up the hydrogen chloride formed in the condensation reaction. The reaction proceeds smoothly at room temperature in a. . . ethyl acetate, and the like. The solution of product is separated from the precipitated hydrochloride salt of the

=>

added tertiary **amine** and can be used as such in forming polynucleotide or alternatively can be separated from the solvent and purified as. . .

SUMM . . . acidic compounds to be employed for the purpose of the said activation are preferably mildly acidic and include, for example, amine hydrohalide salts and nitrogen heterocyclic compounds such as tetrazoles, imidazoles, nitroimidazoles, benzimidazoles and similar nitrogen heterocyclic proton donors. The amine hydrohalide salts to be used for the protonation activation are preferably tertiary amine salts, and, preferably, the hydrochloride salts, although hydrobromide, hydroiodide or hydrofluoride salts can also be used. The aforesaid tertiary amines. . .

SUMM When the nucleoside is guanosine, i.e. where B is guanine, the use of amine hydrochlorides is not very effective for the purpose of activation, i.e. by protonation. With those compounds in which B is.

DETD . . . chloro-N, N-dimethylaminomethoxyphosphine [CH.sub.3 O P(Cl) N(CH.sub.3).sub.2] which is used a monofunctional phosphitylating agent. A 250 ml addition funnel was charged with 100 ml of precooled anhydrous ether (-78.degree. C.) and pre-cooled (-78.degree. C.) anhydrous dimethylamine (45.9 g, 1.02 mol). The. . . caps tightened with copper wire. The suspension was mechanically stirred for 2 h at room temperature, then filtered and the amine hydrochloride salt washed with 500 ml anhydrous ether. The combined filtrate and washings were distilled at atmospheric pressure and the.

DETD . . . were employed in condensation with 3'-O-blocked nucleosides to form internucleotide bonds. The phosphoramidites were activated by weak acids such as **amine** hydrochloride salts or tetrazoles.

DETD A 50 ml dropping funnel was **charged** with 31.59 g of N, N-Dimethylaminotrimethylsilane (42.1 ml, 0.27 mol) which wad added dropwise over 1 h under nitrogen atmosphere. . .

DETD . . . tetrazolide. The gum resulting from the final re-evaporation is dissolved in THF (2 ml). A solution of the selected secondary amine 0.9 mmole) in THF (2 ml) is then added dropwise with stirring at -78.degree. C. to the nucleoside phosphomonochloridite. After. . .

=> d his

(FILE 'HOME' ENTERED AT 10:12:59 ON 18 DEC 2002)

9 S L32 AND CHARG?

```
FILE 'BIOSIS, MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 10:13:34 ON
     18 DEC 2002
         343861 S NUCLEIC ACID
L1
             2 S L1 AND POSITIV? (3A) CHARGE TAG (3A) NUCLEIC ACID?
L2
L3
             21 S L1 AND POSITIV? (4A) CHARG? (3A) TAG?
            19 S L3 NOT L2
L5
            19 DUP REM L4 (0 DUPLICATES REMOVED)
           109 S L1 AND POSITIV? (4A) LABEL
L6
          108 S L6 NOT L5
L7
           92 S L7 AND PHOSPHAT?
L8
L9
           92 DUP REM L8 (0 DUPLICATES REMOVED)
L10
           22 S L9 AND POSITIV? (4A) CHARG?
           1 S POSITIV? (3A) CHARG? (3A) LABEL? (4A) TERMINAL (4A) (NUCLEIC
L11
L12
            1 S L11 AND POSITIV?
L13
          110 S MASS TAG
            50 S L13 AND OLIGONUCLEOTIDE?
L14
            43 S L14 AND LABEL?
L15
            21 S L15 AND TERMINAL
L16
L17
           21 DUP REM L16 (0 DUPLICATES REMOVED)
           1 S POSITIV? CHARG? LABEL? OLIGONUCLEOTIDE?
L18
             1 S POSITIV? (4A) CHARG? LABEL? (3A) OLIGONUCLEOTIDE?
L19
          117 S POSITIV? (5A) (LABEL? OR TAG?) (4A) OLIGONUCLEOTIDE?
L20
            31 S L20 AND AMINE
L21
L22
           23 S L21 AND AMMONIUM
L23
             2 S L22 AND PHOSPHORAMIDITE
L24
           21 S L22 NOT L23
           25 S POSITIV? (3A) CHARG? (3A) PHOSPHORAMIDITE?
L25
           25 DUP REM L25 (0 DUPLICATES REMOVED)
L26
           21 S POSITIV? CHARG? LABEL?
L27
           16 S L27 AND NUCLEIC ACID
L28
           1 S L28 AND POSITIV? (2A) PHOSPHORAMIDITE
2 S POSITIV? (A) CHARG? PHOSPHORAMIDITE
L29
L30
          596 S PHOSPHORAMIDITE/TI
L31
           43 S L31 AND AMINE
L32
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L33